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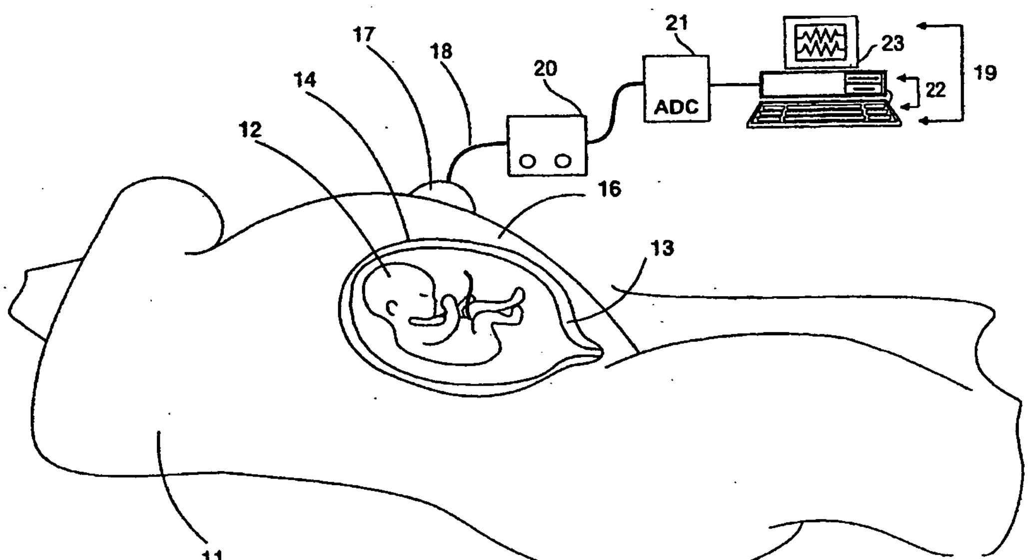

(57) Abstract

A method and apparatus is presented for recording uterine electrical activity from the surface of the abdomen or vagina for the purpose of diagnosing contractile patterns of the uterus in pregnant and nonpregnant patients. The present invention includes surface electrode (17), leads (18), amplifier (20), ADC (21), computer (22), and monitor (23).

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DESCRIPTION

METHOD AND APPARATUS FOR ANALYZING UTERINE ELECTRICAL ACTIVITY FROM SURFACE MEASUREMENTS FOR OBSTETRICAL DIAGNOSIS

BACKGROUND OF THE INVENTION

This invention relates to a method and apparatus for recording uterine or vaginal electrical activity. More specifically, the invention relates to a method and apparatus useful for determining the contractility of the uterus by recording spontaneous, mechanically or electrically stimulated, or drug-evoked electrical activity of the myometrium of the uterus from the abdominal or vaginal surface. The invention further relates to the analysis of surface electromyographic data corresponding to uterine electrical activity for obstetrical diagnosis.

Presently there is no objective manner with which to evaluate the contractility of the uterus. This is true either in nonpregnant patients where hypercontractility is associated with dysmenorrhea or in pregnant patients where the uterus is sometimes active prior to term. Normally the uterus is quiescent in nonpregnant women and during most of pregnancy. However, at the end of pregnancy the myometrium undergoes a series of changes that lead to synchronous, rhythmic uterine contractions (labor). The diagnosis of labor is the most significant problem faced by obstetricians. In addition, preterm labor, which occurs in about 10% of pregnant patients, is difficult to diagnose. Frequently term or preterm labor require adjuvant therapy to either stimulate or inhibit contractility of the uterus.

Since there is some minor spontaneous uterine activity at all times during pregnancy, it is often not possible to distinguish between this physiological activity and term or preterm labor. The state of the cervix is commonly used as a predictor of labor. However, the softening of the cervix occurs relatively late in labor. In addition, labor and changes in the cervix can occur independently. Alternatively the frequency of contractions is used to diagnosis labor, sometimes recorded with a tocodynamometer. However, these methods give only crude subjective estimates of uterine contractility.

The uterus does not contract vigorously throughout most of pregnancy and this provides a tranquil environment for the growing fetus. At term the uterus normally begins to contract forcefully in a phasic manner (labor) to expel the fetus. Contractions of the uterus are directly proportional to the underlying electrical activity of the muscle. The frequency, duration and magnitude of a uterine contraction are directly proportional respectively to frequency of bursts of action potentials, the duration of a burst of action potentials, and the propagation (also referred to as conduction) of action potentials over the uterus and the recruitment of muscle cells. A similar situation exists in heart muscle although heart and uterine muscle are different with respect to structure and configuration of the action potentials. The action potentials are accompanied by the influx of calcium into the muscle cells to activate the contractile apparatus.

Thus, by recording uterine electrical activity one can assess the contractility of the myometrium. Similar technology is used to record cardiac electrical activity to determine the normal or abnormal function of the heart.

Many studies have previously recorded uterine myometrial electrical activity using electromyography (EMG) where electrodes are placed directly on the uterus. These studies show that the myometrium generates little electrical activity prior to labor but activity increases tremendously during labor reflecting the mechanical events. Studies of interest are demonstrated in publications by Csapo, Chapter 43, "Force of Labor," *Principles and Practice of Obstetrics and Perinatology*, Ed. L. Iffy and H.A. Kaminetzky Publishing, John Wiley and Sons 761-799, 1981; Garfield et al., "Control of Myometrial Contractility: Role and Regulation of Gap Junctions," Oxford Rev. Reprod. Biol. 10:436-490; 1988; Wolfs and Van Leeuwen, "Electromyography observations on the human uterus during labor," Acta Obstet. Gynecol. Scand. [Suppl.] 90:1-62, 1979; and more recently by Devedeux et al., "Uterine Electromyography: A Critical Review," Am J. Obstet. Gynecol, 169:1636-1653, 1993. One may measure and use uterine EMG activity by direct contact with the uterus to predict normal and abnormal uterine contractions. However, it is not practical to place electrodes directly on the uterus. To do this under the present level of understanding one must surgically implant electrodes on the uterine surface or introduce a catheter electrode through the vaginal canal and puncture the fetal membranes.

It would be desirable to record uterine EMG activity from the abdominal or vaginal surface. However, previous studies of electrical activity of the uterus recorded with electrodes placed on the abdominal surface have failed to record bursts of action potentials from the uterus and generally show no association of uterine electrical activity with contractility. Studies of interest are included in the above-noted publications by Wolfs and Van Leeuwen, and by Devedeux et al. Wolfs and Van Leeuwen summarized all studies prior to 1979 and

concluded that "it has never been clearly shown that the potential fluctuations obtained by means of electrodes attached to the abdominal wall, do indeed represent the electrical activity of the uterus." (Page 7.) Similarly, Devedeux et al state that abdominal monitoring of uterine electrical activity "requires further investigation." (Page 1649.)

Part of the difficulty in interpretation of electrical activity recorded from the uterus lies in the fact many investigators, including Wolfs and Van Leeuwen and Devedeux et al. have failed to recognize that action potentials drive the uterus to contract. Action potentials are not responsible for contraction of some smooth muscle tissues such as airway muscle and some vascular muscles and therefore many researchers confound the uterus with other smooth muscle tissues. Thus, many of these studies have attempted to correlate electrical activity with mechanical contractions in order to show that electrical activity is responsible for contractions. However, no study has measured uterine and surface EMG simultaneously and correlated these to contractions. Furthermore, it is now clear (from publications by Marshall, "Regulation of Activity in Uterine Smooth Muscle," Physiol. Rev. 42:213-227, 1962; Csapo, Chapter 43, "Force of Labor," *Principles and Practice of Obstetrics and Perinatology,* Ed. by L. Iffy and H.A. Kaminetsky, John Wiley & Sons, 761-799, 1981; Garfield et al., "Control of Myometrial Contractility: Role and Regulation of Gap Junctions," Oxford Rev. Reprod. Biol, 10:436-490, 1988; Garfield, Chapter 3, "Role of cell-to-cell Coupling in Control of Myometrial Contractility and Labor," *Control of Uterine Contractility*, Ed. R.E. Garfield and T. Tabb, CRC Press, 39-81, 1994), that action potentials activate the uterus to contract and that by measuring uterine electrical activity one can indirectly estimate contractility.

SUMMARY OF THE INVENTION

The present invention presents a method and apparatus for recording uterine electrical activity from the surface of the abdomen or vagina for the purpose of diagnosing contractile patterns of the uterus in pregnant and nonpregnant patients. The present invention provides data analysis techniques for analyzing electromyographic data measured from the surface of a patient to characterize uterine activity.

A feature of the present invention is the measurement *in vivo* of the electrical and therefore the mechanical activity of uterine muscle tissue, to produce a more quantitative, comprehensive and analytical framework of the tissue by transferring information from the tissue to a computer memory for automatic analysis and for display on a monitor for assessment by an attending physician or other party interested in monitoring the tissue.

The present invention is applicable to a wide range of obstetrical, gynecological and other conditions. One such application is defining the state of the uterus during term and preterm labor. Another application is monitoring the nonpregnant uterus for indication of conditions such as infertility and uterine pathology in cycling women. The method and apparatus are also valuable for use in connection with other tissues other than the uterus such as tests of bladder function during urination or similarly, evaluation of the bowels during defecation.

The method and apparatus of the present invention includes algorithms for the systematic analysis of electrical signals recorded from the abdominal surface.

Such processing comprises integration of signals, frequency analysis, 3-dimensional mesh plots, vector analysis, fast wavelet transform, and joint time-frequency characteristics. These techniques and apparatus are appropriate for use in the a clinic or through communication lines for use as a remote or "home" uterine monitoring unit. As such, uterine electrical activity may be measured at a remote location. Data from these measurements may be recorded for later processing at a central or remote facility, or it could be processed on-line over communications lines, such as telephone lines or radio frequencies. Further, the present invention can be used to predict successful treatment for cases where either the uterus fails to develop forceful contractions at term or begins to contract pre-term.

In accordance with an embodiment of the invention, recording electrodes are placed at various points on the abdominal surface of a pregnant patient. The electrodes are connected to an amplifier to amplify the electrical signals and in turn the amplifier is linked to a computer for analysis and display of the signals. The signals detected by the electrodes are surveyed to provide measurements indicative of spontaneous electrical activity. The computer contains software to facilitate this analysis of the signals.

The above described electrodes may alternatively be placed on the vaginal wall. This may be particularly useful for monitoring electrical activity in early pregnancy and in nonpregnant women where the uterus is small and not likely to produce strong EMG signals that propagate to the abdominal surface, but are transferred down the reproductive tract to the vagina.

In particular, the present invention contemplates a method of analyzing surface electromyographic data to

characterize uterine activity, comprising applying action potential measuring electrodes to an abdominal surface of a patient; measuring electromyographic signals produced by the electrodes; analyzing frequency components of the electromyographic signals; and characterizing uterine activity of the patient based on the analysis of frequency components. As a further embodiment, the method also includes predicting treatment for the patient based on the characterization of uterine activity, in particular this treatment may be pharmacologically inducing or inhibiting labor in the patient.

The invention also contemplates the stimulation of the vagina of the patient while the electromyographic signals are being stored. This stimulation permits the assessment from the stored electromyographic signals for the phenomenon of conduction, and permits the diagnosis of labor as a function of the signals. The stimulation of the vagina may either be electrical, mechanical or pharmacological, for example through the cutaneous introduction of oxytocin to the patient.

Other further embodiments contemplate isolating high frequency components (F2) within the electromyographic signals; isolating a fast wave component (FW) within the high frequency components (F2); determining a low-frequency (FW_L) domain, including low-frequency components within the fast wave component (FW), and a high-frequency (FW_H) domain, including high-frequency components within the fast wave component (FW); and determining a relationship between the low-frequency (FW_L) domain and the high-frequency (FW_H) domain indicative of an obstetrical diagnosis. This relationship can be indicative of pre-term or term uterine activity.

Still further embodiments of the present invention contemplate determining power density spectral characteristics of the frequency components of the electromyographic signals; and generating a 3-dimensional mesh plot of the power density spectral characteristics, the plot displaying energy levels versus frequency versus time of pregnancy.

An alternative embodiment of the present invention, contemplates a method of analyzing surface electromyographic data to characterize uterine activity, comprising applying six pairs of action potential measuring electrodes to a surface of a patient; measuring electromyographic signals produced by the electrodes; analyzing the electromyographic signals; determining potential vector characteristics of the electromyographic signals to identify a direction of propagation of uterine electrical activity; and characterizing uterine activity of the patient based on the potential vector characteristics. This potential vector can be indicative of a obstetrical diagnosis, including pre-term or term uterine activity.

The apparatus of the present invention includes at least one electrode (unipolar, bipolar, etc) that is applicable to an abdominal surface of the patient under analysis, an analog-to-digital converter, that is connected to the electrodes, and that converts electromyographic signals produced by the electrodes into digitized data which are indicative of electromyographic signals, a memory for storing the digitized signals, and a programmed computer for analyzing the stored digitized signals and for providing a characterization of uterine activity.

An alternative embodiment contemplated by the present invention is an apparatus for recording and

analyzing uterine electrical activity from the abdominal surface, comprising at least one action potential measuring electrode applicable to an abdominal surface of a patient under analysis; an analog-to-digital converter, connected to the at least one electrode, for converting electromyographic signals produced by the electrode into digitized data indicative of the electromyographic signals; a memory for storing the digitized signals; and a programmed computer for analyzing frequency components of the stored digitized electromyographic signals, and for providing an indication of uterine electrical activity of the patient under analysis as a function of the stored digitized signals. A still further embodiment contemplates an apparatus wherein the programmed computer is used further for determining power density spectral characteristics of the frequency components of the electromyographic signals.

The present invention further contemplates an apparatus in the form of a remote uterine monitoring system for analyzing surface electromyographic data to characterize uterine activity, comprising a remote uterine monitor and a central programmed computer in communication with the remote uterine monitor for analyzing stored digitized electromyographic signals, and for providing an indication of uterine electrical activity of the patient under analysis as a function of the stored digitized signals. The remote uterine monitor includes at least one action potential measuring electrode applicable to an abdominal surface of a patient under analysis; and a remote analog-to-digital converter, connected to the at least one electrode, for converting electromyographic signals produced by the electrode into digitized data indicative of the electromyographic signals.

In a further embodiment, the remote uterine monitor and the central programmed computer communicate on-line through a telephone line. In a still further embodiment, the remote uterine monitoring system also includes a remote storage device for recording the digitized electromyographic signal data, and wherein the central programmed computer communicates with the remote uterine monitor off-line through the remote storage device.

These and other features and advantages of the present invention will become apparent to those of ordinary skill in this technology with reference to the following detailed description and appended drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Various features and attendant advantages of the present invention will be more fully appreciated as the invention becomes better understood when considered in conjunction with the accompanying drawings, in which like referenced characters designate the same or similar parts throughout the several views, and wherein:

FIG. 1 is a side view, partially in phantom, showing the recording apparatus in accordance to the present invention attached to the abdominal wall of a pregnant patient.

FIG. 2 is an enlarged view of the surface electrodes used in FIG. 1 in accordance with the present invention.

FIG. 3 is an illustration of two bursts of action potentials of an EMG signal.

FIG. 4A, FIG. 4B, FIG. 4C, FIG. 4D and FIG. 4E are flow charts of the method of the present invention.

FIG. 5, FIG. 6, FIG. 7, FIG. 8, FIG. 9, FIG. 10, FIG. 11, FIG. 12, FIG. 13 and FIG. 14 are graphs of EMG signals, illustrating the present invention.

FIG. 15 is a flow chart of a further embodiment of a data processing technique according to the present invention.

FIG. 16 is a diagram of electromyogram frequency components.

FIG. 17 is a graph of a burst of action potentials recorded from the abdominal surface of a pregnant patient.

FIG. 18 is a graph of a spectral density curve.

FIG. 19A and FIG. 19B are a burst of action potentials recorded from a rat abdominal surface, and a spectral analysis of this burst, respectively.

FIG. 20A and FIG. 20B are a burst of action potentials recorded from a human abdominal surface, and a spectral analysis of this burst, respectively.

FIG. 21 is a system for reducing noise in electrical activity signals in the present invention.

FIG. 22A, 22B, 22C, 22D, 22E and 22F are graphs of spectral analyses for bursts of action potentials recorded from a rat abdominal surface.

FIG. 23A, 23B, 23C, 23D, 23E, 23F and 23G are graphs of spectral analyses for bursts of action potentials recorded from a human abdominal surface.

FIG. 24 is a schematic diagram of the placement of 6 pairs of electrodes for a vector potential analysis.

FIG. 25 is an illustration of a potential vector.

FIG. 26 is a diagram of an application of the present invention as a remote or "home" uterine monitoring system.

DETAILED DESCRIPTION

Referring now to FIG. 1, there is shown schematically a pregnant patient 11 with a fetus 12 retained within the uterus 13. The uterine wall 14 is primarily configured of muscle tissue and is disposed proximate the abdominal wall 16 of the patient 11. In accordance with the principles of the present invention, electrodes 17 are placed on the exterior of the patient 11 on the abdominal wall 16. The electrodes 17 have leads 18 that are connected to a recording apparatus 19 including an amplifier 20, analog-to-digital converter (ADC) 21, computer 22 and monitor 23.

In accordance with the principles of the present invention, the uterus 13 of the pregnant patient 11 is monitored for electrical activity from signals detected on the surface of the abdomen. The signals (EMG) are amplified by amplifier 20, digitized by ADC 21, and displayed on a monitor 23. The signals are also stored in the memory of computer 22 for analysis of the frequency duration and other characteristics of the action potentials.

In accordance with one embodiment of the present invention, ADC 21 may be, for example, a Data-Pack II A/D board, available from Run Technologies, or a MacLab A/D

board, available from MacLab Division of AD Instruments. Amplifier 20 may be, for example, a Grass polygraph recorder, Mode #7D with DC amplifiers, available from Grass Instruments, or a Gould amplifier and recorder Model TA240, available from Gould Instruments, or a MacLab amplifier for Macintosh computers, available from the MacLab Division of AD instruments. Computer 22 with monitor 23 may be, for example, any IBM PC compatible computer, preferably with a 486-type microprocessor and color display, or a Macintosh IIci computer with display, or a Mackintosh Powerbook lap-top computer, or an IBM lap-top computer, or any other equivalent computer and monitor.

Electrodes 17 may be, for example, stainless steel clips or cups, for example, various models available from Hewlett-Packard, silver or platinum clips or cups, or they may be a Bard catheter with electrodes for vaginal recording, available from Bard Reproductive Sciences.

Although specific examples have been given for the various hardware components shown in FIG. 1, it will be understood that different hardware components may be used, without departing from the spirit and scope of the present invention.

Referring also to FIG. 2, an enlarged side view of the electrodes 17 is shown, that are used in contact with a patient's abdominal wall. The electrodes 17 are bipolar (or tripolar) comprised of silver or platinum, and are spaced about 1 cm apart. Leads 18 from the electrodes 17 are connected to amplifier 20.

The amplifier 20 includes controls for amplifying or attenuating the signals and also filters for elimination of some of the high or low frequency noise. The amplifier is, for example, a battery powered ac/dc

differential amplifier with the following approximate specifications:

Gain, AC and DC	x100, x1,000 & x10,000
Input resistance	10^{12} ohms typical
Leakage current	50 pA typical
Common Mode Rejection	100,000:1 min @ 60 Hz
Noise, input shorted	10μV p-p, 1 Hz-0kHz
Low Freq filter settings	0.1, 1.0, 10, 300Hz
High Freq filter settings	0.1, 1.0, 3.0, 10kHz
Output resistance	220 ohms

The computer 22 and monitor 23 may be of conventional PC design with software and hardware to digitize the signals. The computer 22 is programmed with software to enable computer 22 to store, display and analyze the signals. The operation of computer 22, in accordance with the present invention, is discussed below in detail with reference to the flow charts of FIG. 4A, 4B, 4C, 4D and 4E.

Referring also to FIG. 3, shown are typical bursts 31 that are composed of multiple action potentials 32 recorded from the surface of a patient's abdomen 16 from electrical activity of the uterus 13 and that correspond to the overlying contractility of the uterus 13 (see also, FIG. 1). Various parameters are measured from the bursts and from the action potentials, and are used for diagnostic purposes in accordance with the present invention. These parameters include: Frequency of bursts($1/T_B$), number of bursts per unit time (N_B), duration of bursts (D_B), quiescent periods between bursts (Q_P), number of action potentials in each burst (N_P), and characteristics of the action potentials including, frequency of action potentials ($1/T_P$), duration of action potentials (D_P), magnitude of action potentials (M_p), rate of rise of action potentials (R_p, i.e. slope of the depolarization of action potentials, dv/dt).

Referring now to FIG. 4A, 4B, 4C, 4D and 4E, presented are flow charts depicting the operation of the apparatus of FIG. 1, in accordance with the present invention. In practice, the flow charts of FIG. 4A, 4B, 4C, 4D and 4E are embodied in a computer program used to control the operation of computer 22 of FIG. 1. Beginning in step 41, computer 22 acquires EMG signals produced by electrodes 17, which have been amplified by amplifier 20 and digitized by ADC 21. In step 42, digitized versions of the EMG signals are stored in the memory of computer 22.

Control then passes to step 43 where the stored EMG data is analyzed to assess parameters reflecting groups or bursts of action potentials present in the stored EMG signal. These analysis steps are shown in more detail with reference to FIG. 4B. Control then passes to block 44 wherein the stored EMG signal is analyzed to determine parameters characterizing the individual action potentials within the stored EMG signal. The details of the action potential analysis is shown in FIG. 4C.

Control then passes to step 46 where probability analysis is conducted on the EMG signal characteristics determined in steps 43 and 44. The details of this probability analysis are shown with reference to FIG. 4D.

Control then passes to decision block 47 where, based upon the probability analysis performed in step 46, it is determined whether the stored EMG signal reflects normal or abnormal uterine progression. The details of this diagnostic decision are shown below with reference to FIG. 4E. If normal progression is concluded by decision block 47, control passes to block 48 wherein the normal progression is characterized as either non-labor, pre-labor or labor based upon characteristics of the bursts and action potentials. If abnormality is

concluded by decision block 47, control passes to block 49 where the abnormality is characterized as preterm labor, dystocia or other abnormalities based upon characteristics of abnormal bursts and action potentials.

Referring now to FIG. 3 and FIG. 4B, the details of the analysis of burst activity conducted within block 43 of FIG. 4A are presented. Beginning in step 51, the frequency of each burst ($1/T_B$) is determined by estimating the number of bursts per unit time, control then passes to block 52 where the duration of each burst (D_B) is determined by measuring the time from the first action potential of the burst until the final action potential of the burst. Then, in block 53, the quiescent periods (Q_P) between the bursts are determined from measurements of the last action potential in a burst to the first action potentials in another burst. Then, in block 54, the number of action potentials in each burst (N_p) are determined Control is then returned to the flow chart of FIG. 4A.

FIG. 4C presents the details of the analysis of action potential performed by block 44 of FIG. 4A. Beginning in block 61, the frequency of the action potential ($1/T_p$) is determined by estimating the number of action potentials per unit time within each burst. Then, in block 62, the duration of the action potentials (D_P) is determined by measuring the time from depolarization to repolarization. Control then passes to block 63 where the magnitude of the action potentials (M_P) is determined from measurements of the peak voltage of the depolarization. Control then passes to block 64 where the rate of rise of the action potentials (R_p) is determined by determination of the slope dv/dt of depolarization. Conduction is estimated in a known manner from the rate of rise of action potentials (R_p). In general, the greater the rate of rise, R_p, the higher

the conduction. Conduction may also be estimated from analysis of data when more than one surface electrode is used and time between bursts from separate electrodes is estimated or after vaginal stimulation (see below). Control then returns to the flow chart of FIG. 4A.

FIG. 4D shows details of the probability analysis performed by block 46 of FIG. 4A. Beginning in block 71, the mean of each of the measured parameters is determined (see also, FIG. 4B and FIG. 4C), and the standard deviation of each of the parameters is calculated.

FIG. 4E presents the details of the diagnosis step (block 47). Data from burst and action potential probability analysis (block 46) pass to blocks 81 and 82 respectively and recorded burst and action potentials are compared to known normal ranges of values. Estimates for normal values for the measured parameters for action potentials and bursts of action potentials for labor patients are presented in the following tables.

ACTION POTENTIALS

Frequency:	1/second
Duration:	100 milliseconds
Amplitude:	1 millivolt

BURSTS

Frequency:	0.5-2.0/minute
Duration:	10-30 seconds
Action Potentials/Burst:	20

For non-labor patients, considerably lower values for the measured parameters for action potentials and bursts of action potentials are considerably lower than the values presented in the above tables, with the exception of burst duration which may actually be larger. For values either higher or lower than normal for burst

or action potential data, the computer recognizes these as abnormal and passes control to block 49. If burst or action potential parameters are within normal limits, the information passes to block 48. The calculated standard deviations for the measured parameters are used to determine whether the calculated parameter means for statistically different or the same as normal values.

While utilization of the apparatus and method has been described above as particularly useful for monitoring the uterine wall during pregnancy, the instrument can also be used to measure electrical activity from the vagina that propagates or conducts from the uterus. This is particularly useful in early pregnancy or in nonpregnant patients where the uterus is small and not in contact with the abdominal wall. In addition, it is within the scope of this invention to utilize the apparatus and method thereof for medical and biological procedures other than uterine wall monitoring, such as, for example bladder or bowel function.

From the foregoing description, one skilled in the art may easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, may make various changes and modifications of the invention to adapt it to various usages and conditions.

FIG. 5, FIG. 6, FIG. 7, FIG. 8, FIG. 9, FIG. 10, FIG. 11, FIG. 12, FIG. 13 and FIG. 14 illustrate use of the present for monitoring uterine electrical activity. To produce the graphs of FIG. 5, FIG. 6, FIG. 7, FIG. 8, FIG. 9, FIG. 10, FIG. 11, FIG. 12, FIG. 13 and FIG. 14, bipolar electrodes were placed on the abdominal surface of pregnant rats to monitor EMG activity in accordance with the present invention. In addition, in order to demonstrate the efficacy of the present invention

relative to prior, more invasive, procedures, stainless steel electrodes were implanted directly on the uterus and/or vagina wall surface, and, a pressure transducer (specifically, a Model SPR-524 transducer available from Millar Instruments of Houston, Texas) was placed in the uterus. The apparatus for recording was identical to that described above. The above described invention is designed for use mainly in humans or domestic animals whereas the following FIG. 5, FIG. 6, FIG. 7, FIG. 8, FIG. 9, FIG. 10, FIG. 11, FIG. 12, FIG. 13 and FIG. 14 represent data obtained from rats. The instrumentation is essentially the same for both species.

FIG. 5, FIG. 6, FIG. 7, FIG. 8, FIG. 9, FIG. 10, FIG. 11, FIG. 12, FIG. 13 and FIG. 14 illustrate the correlation between the EMG signals recorded by the abdominal surface electrodes of the present invention, and signals recorded from uterus electrodes surgically implanted in the uterus.

FIG. 5, FIG. 6 and FIG. 7 show EMG activity (electrical activity of the uterus) (Channels 1 and 2) and pressure (Channel 3) recorded simultaneously directly from the uterine wall (Channel 1) and from the abdominal surface (Channel 2) of pregnant rats. Pressure (Channel 3) was measured from an intrauterine pressure device. Note that on days 18 and 21 of gestation (FIG. 5 and FIG. 6) bursts of electrical activity are small and do not always correspond on the surface and uterus (FIG. 5, Channels 1 and 2), but do coincide with small uterine contractions (FIG. 5, FIG. 6 and FIG. 7, Channel 3). On the other hand, at term during delivery (FIG. 7) the EMG bursts signals from both the uterus and abdominal surface are of high amplitude and correlate with large pressure changes.

These studies indicate that uterine EMG activity is low prior to term and that it increases dramatically during labor and delivery. Furthermore, these data show that uterine electrical activity may be recorded from the abdominal surface (Channel 2) to give an adequate representation of either the uterine electrical or mechanical activity.

FIG. 8 shows EMG and pressure recordings from an animal during labor at term before and after treatment with oxytocin. Note that the bursts (Channels 1 and 2) coincide to low pressure changes (Channel 3) prior to oxytocin. Following IV infusion of oxytocin the EMG activity as recorded on the uterus (Channel 1), and abdominal surface (Channel 2) increase substantially and correspond to the large pressure changes in the uterus. These results indicate that electrical activity recorded from the surface of the abdomen (Channel 2) accurately mirrors changes in uterine EMG activity (Channel 1) and uterine pressure (Channel 3).

FIG. 9 shows an expanded portion of an EMG burst recorded from the uterus (Channel 1) and abdominal surface (Channel 2). Note that the individual action potentials within the bursts correspond between those recorded from the uterus and surface.

FIG. 10 illustrates EMG activity recorded from the uterus (Channel 1), abdominal surface (Channel 2) and activity of the heart (recorded with external electrodes placed on the chest) (Channel 3). Note that cardiac action potentials occur regularly with a frequency which matched the heart rate (300 to 400 beats per minute). In contrast bursts of action potentials from the uterus recorded with both uterine and abdominal surface electrodes occur periodically. Note that a minor signal from the cardiac potentials appears in the EMG signals

from the uterus and uterine signals overlap with some signals from the heart. This information shows that one can record action potential bursts from the uterus with surface electrodes on the abdomen with little interference from the heart.

FIG. 11 demonstrates EMG recordings from the uterus and abdominal surface in conscious rats (FIG. 5, FIG. 6, FIG. 7, FIG. 8, FIG. 9, FIG. 10 and FIG. 12 show data from anesthetized animals). Shown are corresponding bursts of EMG activity demonstrating that it is possible to record uterine electrical signals from the abdominal surface from conscious animals.

FIG. 12 shows EMG recordings from the uterus (Channel 1) and vagina surface (Channel 2) and intrauterine pressure (Channel 3). Note the correspondence between uterine and vaginal EMG activity with accompanying changes in intrauterine pressure. These studies indicate that it is possible to record uterine EMG activity from the vaginal wall.

FIG. 13 and FIG. 14 depict a portion of EMG signals recorded from the uterus (Channel 1) and from the vaginal surface (Channel 2), indicating that when the vagina is stimulated mechanically during labor, signals are propagated (conducted) to the uterus (FIG. 13), whereas when the vagina is mechanically stimulated prior to term, signals are not conducted to the uterus (FIG. 14). This assessment of conduction may be used to indicate or diagnose a state of preparation for labor.

The present method and apparatus may also be used to measure normal and abnormal function of other smooth muscle tissue, such as that of the bladder and lower gastrointestinal tract. Both organs depend upon smooth muscle contractility to perform their respective

functions. Thus, electrical activity of the bladder and bowel may be registered from the abdominal surface during respective urination or defecation, in order to estimate appropriate and abnormal electrical activity of these organs.

The analysis of EMG activity by abdominal surface recording to determine uterine contractility is further discussed in Buhimschi and Garfield, Uterine Contractility as Assessed by Abdominal Surface Recording of EMG Activity, approved for publication in AM. J. OB/GYN.

The present invention may also be used as a remote or "home" uterine monitoring system. FIG. 26 shows a diagram for an embodiment of a remote monitoring system 2600. Uterine electrical activity may be measured at a remote location, such as in the privacy of one's home, utilizing remote monitor 2602. The data from these measurements may be sent to storage device 2604 so that it may be recorded for later use. This data from storage device 2604 may then be sent to central data processor 2606 at a central facility, such as a hospital. The data from storage device 2604 may also be analyzed by remote data processor 2610 that may also be located in a "home" environment. Alternatively, data from measurements of uterine electrical activity may be processed on-line in real-time by central data processor 2606 or remote data processor 2610. Communication between remote monitor 2604 and central data processor 2608 can be accomplished through telephone lines, radio frequency links, or other remote communication techniques. After the electrical data is processed by central data processor 2606 or remote data processor 2610, a diagnosis 2608 may be made.

The present invention may also be used to predict treatment for a pregnant woman. The data signals

collected can be analyzed by the present system and compared to existing norms to indicate the appropriate pharmacological treatment depending upon the uterine activity. For example, when signal levels are low and indicative of non-labor, a term patient can be treated in such a fashion pharmacologically to induce labor (i.e., oxytocin, prostaglandins, etc.). When signal levels are high in a patient prior to term (i.e., pre-term labor) treatment can consist of use of uterine inhibitors to suppress labor (e.g., tocolytic agents, β-agonists, calcium channel blockers, etc.). As one of skill would understand, other obstetric diagnosis treatments could be predicted using the present invention.

From the techniques described above, digital analysis techniques have now been developed and further improved to analyze further the surface EMG activity for obstetrical diagnosis and characterization of uterine activity. FIG. 15 shows a flow-chart for an embodiment of a method according to the present invention. Method 1500 for analyzing surface electromyographic data to characterize uterine activity includes process steps 1502, 1504, 1506 and 1508. In step 1502, EMG signals are first acquired. After this data is obtained, the EMG signals are analyzed in step 1504. Once processed and analyzed, parameters are determined from the EMG signals that are indicative of a obstetrical diagnosis in step 1506. Finally, a diagnosis is made or predicted in step 1508. Within this general framework, a wide variety of data analysis techniques may be employed to analyze EMG signal for obstetrical diagnosis.

These analysis techniques may include: (1) power-density spectral analysis based upon 3-dimension mesh plots (e.g., energy level vs. frequency vs. time of pregnancy), (2) potential vector analysis, and (3) other analytical techniques, such as integration of the EMG

signals to provide approximate total energy within a burst of action potentials, fast wavelet transform analysis, and joint time-frequency analysis.

These analytical systems provide important information on EMG that can be used for diagnosis. These systems are based upon the recording of uterine electrical activity from the abdominal surface as described above. The abdominal electromyogram (EMG), or electrohysterogram (EHG), may be analyzed and the resulting analysis used to facilitate the clinical evaluation of uterine activity during pregnancy. The present invention may also be utilized for the early diagnosis of abnormal uterine contractility by analyzing uterine EMG signals. Such diagnoses take advantage of the characteristic that uterine electrical activity gradually changes during the last month of pregnancy until parturition. Weak and localized at the beginning of labor, this electrical activity becomes stronger, rhythmical and well propagated during labor. EMG, therefore, offers much information about both excitation and propagation of uterine activity.

These data analysis techniques also rely upon an unique approach to characterizing EMG frequency components of a burst of action potentials. FIG. 16 shows the EMG frequency components of a burst of action potentials recorded from a human uterus. A burst of action potentials is shown in FIG. 17, which provides an amplitude versus time graph of a burst of action potentials recorded from the abdominal surface of a pregnant patient.

Referring back to FIG. 16, F1 (less than 0.005 Hz) is representative of low frequency components in the EMG data, such as the periodic occurrence of a burst. During human parturition, the burst frequency corresponds to a

maximum of three contractions per 10 minutes (i.e., maximum F1 = 0.005 Hz). F2 (approximately 0.005 to 3.0 Hz) is representative of high frequency components, such as the intrinsic spike frequency within each burst. F2 frequencies are believed to be more significant than F1 frequencies because they are related to the intensity of the uterine contraction.

F2 can be divided into two distinct activities: a slow wave component and a fast wave component (FW). The slow wave component, ranging from approximately 0.005 to 0.03 Hz, is mainly obtained with abdominal recordings and is likely caused by mechanical artifacts. The fast wave component is of more importance and is the frequency band representative of uterine activity (about 1 Hz for a human). This fast wave frequency spectrum can be recorded in virtually all situations (myometrial or abdominal recordings, parturition of pregnancy).

In turn, this fast wave component contains two specific domains: a low-frequency (FW_L) domain present in any uterine electrical recording and a high-frequency (FW_H) domain. The FW_L domain relates to lower frequency components (e.g., FW_L is in an approximate range from 0.01 to 0.06 Hz) having a longer duration (the duration mean was computed as 74.6 sec). In contrast, labor EMG is related to the presence of "high" frequency components (e.g., FW_H is in an approximate range from 0.06 to 3.0 Hz) having a shorter duration (the duration mean was computed as 59.3 sec).

The relationship between FW_L and FW_H has been found to indicate preterm and term uterine activity. It may also be useful in making other obstetrical diagnosis. This relationship can be expressed by various parameters, including parameters that are not dependent on the individual patient. Thus, these parameters may be used

as differentiation parameters in indicating diagnoses and characterizing uterine activity.

The following data analysis techniques are based upon analyses of EMG signals using various approaches and represent different definitions and calculations of these parameters.

1. <u>Power-Density Spectral Analysis</u>

a. Spectral Analysis Technique

A spectral analysis method may be used to obtain important spectral characteristics of uterine EMG and define some key parameters useful in the differentiation of normal and abnormal uterine activity.

To specify the frequency range that only concerns the previously defined "fast" electrical activity, spectral analysis processing is performed on the phases of EMG corresponding to contractions of the pressure signal. The power density spectrum (PSD) curve which is computed from the filtered "fast" (0.2-3.0 Hz) electrical burst relates to one contraction (see FIG. 17). The pregnancy contraction mainly corresponds to the FW_L frequency band and the labor contraction to the FW_H band. The energy on each of FW_L band FW_H band can be calculated. Defining E_{fwL} as the energy of FW_L band and E_{fwH} as the energy of FW_H, the total energy E_{fw} on the FW band is

$E_{fwL}+E_{fwH}$. The formula is as follows:

$$E_{fwL} = \int_{fl1}^{fl2} P(f)df$$ (FW_L frequency bandwidth is [fl1,fl2] as shown in FIG. 18)

fh2

$$E_{fwH} = \int_{fh1} P(f)\,df$$ (FW_H frequency bandwidth is [fh1,fh2] shown in FIG. 18)

$$E_{fw} = E_{fwL} + E_{fwH};$$

Referring to FIG. 18, which depicts an EMG power spectral density (PSD) curve, the geometrical significance of E_{fwL} and E_{fwH} are the areas under the PSD curve. The physical significance of E_{fwL} and E_{fwH} is the energy of contraction in pregnancy phases. The energies in different pregnancy phases and labor stages are expected to be different. The EMG signals that are processed are discrete signals. Their PSD are also discrete functions. So, E_{fwL} and E_{fwH} can be calculated as follows:

$$E_{fwL} = \sum_{f=fl1}^{fl2} PSD_f,$$

$$E_{fwH} = \sum_{f=fh1}^{fh2} PSD_f,$$

The energy may be dependent on the individual patient. Supposing that the ratio (Re) of E_{fwL} and E_{fwH} is independent of individuals, standard ratios (possibly invariable) may be developed at each different stage of pregnancy, pre-labor and labor. Thus, the following ratio may be particularly useful as a parameter indicative of an obstetrical diagnosis:

$$Re = E_{fwH}/E_{fwL}.$$

Based on this supposition, the ratio in the early pregnancy phase is expected to be smaller than the ratio in later pregnancy and the labor phases. This ratio will increase with the days of pregnancy. This means the E_{fwL} decreased but the E_{fwH} increased. In the normal state, the ratio in a certain phase of pregnancy or labor is expected to be a standard ratio. If the ratio in certain phases of pregnancy is larger than the standard ratio in this phase, the woman may be considered to be in an abnormal pregnancy state (the commencement of premature labor or miscarriage). If the ratio is smaller than the normal ratio, the woman may be in danger and may suffer post-labor or dystocia problems.

Referring to FIG. 19A, FIG. 19B, FIG. 20A and FIG. 20B, they show power density spectra for FW_H components during labor. FIG. 19A is a burst of action potentials recorded from a rat's abdominal surface. FIG. 19B is a power density spectra obtained for the burst shown in FIG. 19A. As evident from FIG. 19B, labor in a rat is indicated by a large frequency component between 2-3 Hz. FIG. 20A is a burst of action potentials recorded from a patient's abdominal surface. FIG. 20B is a power density spectra obtained for the burst shown in FIG. 20A. As evident from FIG. 20B, labor in a woman is indicated by a large frequency component at approximately 1 Hz.

b. Application of Spectral Analysis

The development of spontaneous uterine contractility exists throughout pregnancy, labor, and the early postpartum. Changes in magnitude of uterine activity in relation to duration of pregnancy and to the successive stages of labor and postpartum increases dramatically during labor. These correspond to the tremendous increase in electrical activity (PSD) during labor.

In the examples described below, the whole EMG data was classified as normal or abnormal (pre-labor, miscarriage, post-labor, labor difficulty, etc.) according to the end-result. If a woman finished normal delivery, the whole EMG data was classified as normal, otherwise it was classified as abnormal. After acquiring EMG data, the temporal and spectral characteristics of this data was analyzed for important statistical parameters. The parameters include Re, E_{FWL}, E_{FWH}, duration of contraction, and statistical data, such as correlation coefficient and covariance.

In the study, two Ag-AgCl Beckman electrodes (8mm in diameter, 25mm spaced centers) were placed on the abdominal wall after careful preparation of the skin. They were located on the median vertical axis, halfway between uterine fundus and the symphysis, thus parallel to the more superficial uterine fibers. The ground electrode was located laterally on the hip. These electrode locations, based on common anatomic references, have been found to provide good EMG results.

The MacLab digital signal acquiring system was used to obtain EMG signals. The mechanical effect of uterine contractions were recorded by the existing method of pressure recording with an intrauterine catheter or surface pressure with a tocodynamometer. The pressure recording detects weak contractions in pregnancy. The pressure signal may be simultaneously recorded with the EMG, providing a time reference for the appearance of contractile activity.

c. Filtering to Eliminate Noise

The raw EMG signals can be contaminated by noise. The noise includes respiratory artifact, background noise due to motion, and ECG (material and fetal). Adaptive

Noise Canceling (ANC) and Adaptive Line Enhancer (ALE) methods with the LMS (lease mean squares) adaptation algorithms were used to cut off the noise. The noises were first classified into reference noises and background noise that contaminate the EMG signal according to their frequency range. The frequency range of the EMG fast wave component lies mostly between 0.2Hz and 3Hz. The frequency of respiratory artifacts is around 0.3Hz. Some overlap, therefore, exists between frequencies caused by the respiratory artifacts and the EMG signals. An adaptive noise canceler is used to eliminate the respiratory artifact from the desired uterine EMG measurements.

The ECG signal (from heart activity) frequency range is greater than 2Hz. Thus, there may also be some overlap between ECG and EMG signals. However, this overlapping part of the ECG signal has very low energy. The nonoverlapping part of the ECG can be processed as background noise. Thus, the noises that contaminate the EMG signal are mainly respiratory signals (mostly overlap with EMG) and background noise (including ECG signals).

Referring to FIG. 21, a system for reducing the noise in the EMG signal is shown. In particular, an adaptive filter system is shown, which consists of the Adaptive Line Enhancer (ANE) and the Adaptive Noise Canceler (ANC). The components for these systems are available from Newark Electronics, Chicago, Illinois. Both filters use a LMS (least mean square) algorithm.

In operation, the main signal d_j, which includes the EMG signal or primary signal (s_j), is bandpass filtered with bandwidth 0.2-3.0 Hz before adaptive filtering. An adaptive noise canceler (ANC) is used to filter out respiratory noise (r_j). Here, a respiratory signal is also a reference signal (r_j) of the ANC. A respiratory

reference signal is recorded by positioning a pressure transducer on the chest above the diaphragm. The Adaptive Line Enhancer (ANE) is to eliminate the background noises n_j from the primary signal s_j. The delay, Δ, is chosen as one constant according to practical experiments to decorrelate the periodic and correlated signals s_j and r_j from n_j.

Thus, the Adaptive Line Enhancer (ANE) part of the adaptive system functions as a preprocessing unit to eliminate the background noise n_j. The adaptive noise canceler is used to eliminate respiratory artifacts (r_j). After the processing, an enhanced main EMG signal (s_j) is acquired and may be analyzed.

d. Time and Shape Analysis of Burst Power

The power density spectral analysis does not define differences in power density at different time points within the burst. This is likely important during pregnancy when electrical coupling is poor prior to term as compared with well coupling during labor. In this type of analysis, the power of the burst over time is expressed. Prior to term, this analysis is expected to show a weak initial signal with a peak during the mid-phase of the burst. Because electrical coupling is improved during normal labor, the power per unit time is expected to be maximal with little change from beginning to the end of a burst.

e. Application of Spectral Analysis Technique

To specify the frequency range representative of the previously defined "fast" electrical activity, the spectral analysis is performed on the EMG signal phases corresponding to contractions. The contractions are detected by recording pressure at the same time when the

EMG signals are recorded. The power spectral density is computed in the frequency range 0.2-3.0 Hz with a Kaiser Window Filter. An estimation technique of parametric modeling methods was used to calculate the PSD. Parametric modeling methods include AR (Autoregressive Methods) and ARMA (Autoregressing Moving Average Method).

According to the PSD, the energy on discriminating frequency bands FW_L and FW_H and the energy ratio Re can be calculated. After acquiring a group of Re's, statistical values of Re and its standard deviation (SD) can be calculated. The power spectral analysis (PSD) can be carried further along into coherence analysis if necessary, such as that described in Sica, *et al.*, Respiration-Related Features of Sympathetic Discharges in the Developing Kitten, *Journal Automatic Nervous System*, 44:77-84, 1993; and Sica, *et al.*, Evidence for Central Patterning of Sympathetic Discharge in Kittens, *Brain Research*, 530:349-352, 1990.

Focusing on frequency analysis of the amplitude or energy levels in bursts of action potentials at various times in pregnancy, mesh plots of the "power density" of the bursts of action potentials can be created.

FIG. 22A, FIG. 22B, FIG. 22C, FIG. 22D, FIG. 22E and FIG. 22F represent graphical depictions of power density analyses and 3-dimensional mesh plots for EMG data measured from the uterine activity at a rat's abdomen surface.

FIG. 22A shows a burst of action potentials from the EMG signal, as well as the corresponding intrauterine pressure (IUP) changes, recorded from a pregnant rat at day 22, where the rat was not in labor. FIG. 22C shows a burst of action potentials form the EMG signal, as well as the corresponding intrauterine pressure (IUP) changes,

recorded from a pregnant rat at day 22, where the rat was in labor. Only frequencies between 0.3-50 Hz in the EMG signal are shown in FIG. 22A and FIG. 22C.

FIG. 22B shows a power density spectral analysis of the burst shown in FIG. 22A. For a rat not in labor, no large frequency components are present, except for a component below 0.5 Hz. This component is attributable to respiratory noise or breathing. FIG. 22D shows a power density spectral analysis of the burst shown in FIG 22C. In stark contrast to the frequency components present in FIG. 22B, large frequency components are present in FIG. 22D. Comparing FIG. 22B and FIG. 22D, it is significant to note that the peak frequency of the action potentials occurs between approximately 2-3 Hz in a delivering rat and that very high energy levels occur during labor as compared to a non-delivering rat. It should also be noted that a large frequency component is still present in FIG. 22D below 0.5 Hz, which may again be attributed respiratory noise or breathing.

Referring to FIG. 22E, a mesh plot (energy levels vs. frequency vs. time of pregnancy) is shown that was prepared from many rats at different times in pregnancy. FIG. 22E shows that the energy level was very low (flat) prior to labor at days 18 to 22 NL (NL representing "non-labor"). Energy levels then rose sharply during labor at day 22 L (L representing "labor"). The energy levels then declined rapidly during postpartum days 1-2 pp (pp representing "postpartum").

Referring to FIG. 22F, a combined mesh plot is shown. This mesh plot includes a mesh plot from EMG measurements from a rat for a normal delivery overlapped with a mesh plot from EMG measurements from a rat for a preterm delivery. Preterm delivery was achieved by treating a rat with ZK299 (onapristone) to induce preterm

birth. As evident from FIG. 22F, energy levels for a forced preterm delivery were also greatly increased over a normal pregnancy as shown in FIG. 22E.

The data in FIG. 22A, 22B, 22C, 22D, 22E and 22F, therefore, show that power density spectral analysis of the EMG signals from bursts of action potentials may be used to predict when an animal is in term or preterm labor. The changes in the power density spectra from low to high levels reflect increased excitation and propagation of action potentials in the myometrium during labor and delivery. Thus, the spectral analysis provides a technique for indicating or predicting treatment during pregnancy. Further, these analyses may provide indications of other obstetrical diagnoses.

The techniques described above were also used to measure EMG signals of bursts of action potentials in pregnant women. FIG. 23A, 23B, 23C, 23D, 23E, 23F and 23G represent graphical depictions of power density analyses and a 3-dimensional mesh plot for EMG data measured from the uterine activity at a woman's abdomen surface.

FIG. 23A and FIG. 23B show electrical activity recorded from two sites on the abdominal surface in a patient at 27 weeks of gestation (FIG. 23A) and in a term laboring patient (FIG. 23B). The patient at 27 weeks was progressing normally and appeared for a weekly perinatal visit. She had worked all day and felt minor contractions that corresponded to the EMG activity (arrows in FIG. 23A). Eventually, this patient delivery a healthy boy at term. In contrast, the patient at term labor in FIG. 23B shows high amplitude and frequent (every 1/2 min.) EMG bursts. This patient delivered a normal baby girl about 30 minutes after the above record was made. Comparing 23A and 23B, it is evident that the

frequency and amplitude of EMG bursts are quite different between the term and preterm patients.

FIG. 23A and 23B also provide duplicate readings. The first set was made using large electrodes. The second set was made using small electrodes. Both the small and large electrodes were found to be equally effective.

FIG. 23C shows a burst of action potentials from the EMG signal recorded from a pregnant woman at 27 weeks, where the woman was not in labor. FIG. 23E shows a burst of action potentials form the EMG signal recorded from a pregnant woman at week 42, where the woman was in labor. Only frequencies between 0.3-50 Hz in the EMG signal are shown in FIG. 23C and FIG. 23E.

FIG. 23D shows a power density spectral analysis of the burst shown in FIG. 23C. For a woman not in labor, no large frequency components are present. FIG. 23F shows a power density spectral analysis of the burst shown in FIG 22E. In stark contrast to the frequency components present in FIG. 22D, large frequency components are present in FIG. 22F. Comparing the power spectrum analyses of the EMG bursts from the above patients (FIG. 23D and FIG. 23F), the bursts from the patient at 27 weeks gestation showed low energy levels (FIG. 23D), while the term labor patient demonstrated very high energy with a peak frequency about 1 Hz (i.e., 1 action potential per second) (FIG. 23F). It should also be noted that a large frequency component is present in FIG. 22F below 0.25 Hz, which may be attributed to respiratory noise or breathing.

FIG. 23G shows a power density spectral mesh plot (energy levels vs. frequency vs. weeks of gestation) for EMG measurements of bursts of action potentials from a

pregnant patient during gestation. Analysis of such data for many patients showed very similar results to the rat studies above (compare to FIG. 22E). In particular, it was found that the power density spectrum is relatively low (flat) prior to term labor, but rises dramatically during labor.

The above data indicates that spectral analysis of EMG bursts in women is of considerable value in evaluating the contractile state of the uterus during pregnancy. Information from these analyses can be used to dictate treatment. Patients at term with low power density spectrum score would not be expected to have passed through the series of steps necessary for excitation of the myometrium and, therefore, may require adjuvant treatment to augment labor. On the other hand, patients with a high score, normal for labor, would be predicted to progress without any treatment.

Similarly, spectral analysis may be useful to foretell treatment and outcome of patients thought to be in preterm labor. Patients thought to be in preterm labor that have a low spectrum score might be expected to proceed normally to term. High spectral scores preterm should be coincident with true labor contracts and this information may lead to effective treatment to prevent preterm birth.

Spectral analysis may also be used to estimate the transition from low to high energy levels. Thus this technology may be helpful to monitor patients continuously in order to assess normal or abnormal progress. These methods will also be particularly useful for remote or "home" uterine recordings and monitoring. In this way, patients can easily be instrumented and monitored from a distance via a communications link, such as telephone lines.

2. Potential Vector Analysis Using Vectorhysterograms

A vector analysis of action potentials may also be used to determine useful parameters for obstetrical diagnosis.

The uterine electromyogram is the result of electrical activity generated at the cellular level. The potential at any arbitrary point on the abdominal surface, back and sides from a pregnant woman may be measured and recorded, and the whole uterus can be modeled as a dipole vector. If the vector represents the spread of uterine myometrium excitation, the orthogonal component of the vector can be recorded. The orthogonal vector component $P_x(t)$, $P_y(t)$ and $P_z(t)$ of the vector P and its direction can be determined and analyzed.

a. General Principles

Body surface potential vector analysis is based on Frank's torso experiment model and research results. In the 1950's, Frank shaped a plaster cast of a subject's body, waterproofed it and filled it with saltwater. He then placed a dipole source composed of two electrodes on a rod within the torso model.

From measurements in such experiments, Frank found that the geometrical transfer coefficients that relate the dipole source to each point of the body surface potential $V_n(t)$. Thus for a set of k body surface potentials, there is a set of k equations that can be expressed in matrix from:

$$V = T * P.$$

Here, $V = \{v_1, ..., v_K\}^T$; $T = \{T_1, T_2, T_3\}$; $T_1 = \{t_{11}, ..., t_{1K}\}^T$; $T2 = \{t_{21}, ..., t_{2K}\}^T$; $T_3 = \{t_{31}, ..., t_{3K}\}^T$;

$P = \{P_x, P_y, P_z\}$. V is a K*1 vector, T is a K*3 transfer coefficient matrix. P is the 3*1 time-varying dipole source vector.

Based upon this dipole analysis, and making the dipole source a uterus of a pregnant women, the potential at any point and at the same time can be measured to obtain the orthogonal vector component of the action potentials on an XYZ axis. FIG. 24 illustrates the placement of electrodes on a patient, and a 3-dimensional position of electrodes located on an XYZ axis.

When acquiring the six point potential at any time, the vector component on X, Y axis at this time is also obtained. That is:

$$P_x(t) = V_{x1}(t) - V_{x2}(t);$$
$$P_y(t) = V_{y1}(t) - V_{y2}(t);$$
$$P_z(t) = V_{z1}(t) - V_{z2}(t);$$

It is noted that the direction is that the vector points toward the electrode with higher potential. For example, if $P_x > 0$, then the direction is in X positive direction.

b. EMG Signal Recording and Noise Canceling

Six bipolar pairs of Ag-AgC1 beckman electrodes may be used. They may be arranged on the abdominal surface, sides and back of a patient, as shown in FIG. 24. It is also possible to use a fewer or a greater number of electrodes. Further, other electrodes may be used, such as unipolar, tripolar, etc.

At each point the system records the EMG signal corresponding to the uterine contraction. A Maclab digital signal processing system is used to acquire the

EMG signals at each point. The EMG signal at each point will likely be contaminated by noises. The Adaptive Noise Canceler (ANC) and Adaptive Line Enhancer (ANE) may be used to cut off the noises, as discussed above.

c. Analysis

Six channel EMG signal segments are selected to correspond to the mechanical contact segments of the uterus. Data is then saved into one data file. The data file is then analyzed.

To analyze the data, the orthogonal vector components P_x, P_y and P_z are acquired. According to the orthogonal vector component direction, the tracing of uterine potential vector P(t), can be divided into 8 areas in a 3-dimension space. The rules are as follows:

$P_x(t)$	$P_y(t)$	$P_x(t)$	Area No.
+	+	+	1
-	+	+	2
-	-	+	3
+	-	+	4
+	+	-	5
-	+	-	6
-	-	-	7
+	-	-	8

At each sample time, the system will calculate the direction vector $\{\emptyset_x, \emptyset_y, \emptyset_z\}$ of uterine potential vector P(t) as shown graphically in FIG. 25. $\emptyset_x$ is the angle of vector P(t) with X axis in 3-dimension. $\emptyset_y$ is the angle of vector P(t) with Y axis in 3-dimension. $\emptyset_z$ is the angle of vector P(t) with Z axis in 3-dimension. The formula of calculating the angle is as follow:

$$\emptyset_x = \cos^{-1} (1P_x1/(1P_x1^2 + 1P_y1^2 + 1P_z1^2)^{1/2});$$
$$\emptyset_y = \cos^{-1} (1P_y1/(1P_x1^2 + 1P_y1^2 + 1P_z1^2)^{1/2});$$
$$\emptyset_z = \cos^{-1} (1P_z1/(1P_x1^2 + 1P_y1^2 + 1P_z1^2)^{1/2});$$

The present system may display the vector P(t) tracing in 3-dimension on a computer screen. The user can select the demonstration speed that controls the tracing on screen. When the lower speed is selected, the details of the tracing changes at each sample time can be easily observed. The system supports another method to assist the user to analyze the changes in progression of P(t) at each sample time. At each sample time t_i, the system will determine which area vector $P(t_i)$ should be in according to the rules of area division. The system will draw out the change in progression in order of P(t) as follow:

Time:	t_o	$t_o+\Delta t$	$t_o+2\Delta t$	$t_o+3\Delta t$ ....
Order:	1 to	3 to	5 to	6 to......

Angle: {12,24,53} to {23,54,12} to {3,23,15} to {13,34,60} to...

The results can be printed on a printer. Using this method the vector of activity can be defined, and the origin and direction of spread of activity may also be defined. Using this technique, pacemaker regions and direction of propagation of uterine electrical activity may be identified.

These parameters may then be used to predict treatment of pregnant women or to make other obstetrical diagnoses.

3. <u>Other Data Analysis Techniques</u>

As would be obvious to one of skill in the art, other analytical techniques may be utilized to analyze the uterine electrical activity data described above.

One alternative technique is to integrate the energy measured for a burst of action potentials. Using this technique, the electrical signals in a burst of action potentials recorded from the uterus are first summed (i.e., positive plus negative signals) and the total area under the curve is then integrated. This analysis gives a rough estimate of the energy within a burst of action potentials. It does not, however, account for the length or time component of the data measured. Thus, this analysis could be extended by further dividing the approximate total energy for the burst of action potentials by the total time of the burst to determine the integrated function/time value or energy per unit time for the burst.

Another technique that may be utilized is a fast wavelet transform technique. This technique could be adapted from that described in Cody, *The Fast Wavelet Transform*, Dr. Dobb's Journal (April 1992); Cody, *A Wavelet Analyzer*, Dr. Dobb's Journal (April 1993); and Cody, *The Wavelet Packet Transform*, Dr. Dobb's Journal (April 1994).

A still further technique that may be adapted and utilized is a joint time-frequency analysis. This technique could be implemented utilizing the LabVIEW Joint-Time Frequency Analysis (JFTA) Toolkit available from National Instruments, Austin, Texas.

While the present invention has been presented with reference to particular embodiments, it will be understood that additions, deletions and changes to these embodiments may be made without departing from the spirit and scope of the present invention.

CLAIMS:

1. A method of analyzing surface electromyographic data to characterize uterine activity, comprising:

applying action potential measuring electrodes to a surface of a patient;

measuring electromyographic signals produced by said electrodes;

analyzing frequency components of said electromyographic signals; and

characterizing uterine activity of said patient based on said analysis of frequency components.

2. The method of claim 1, further comprising:

stimulating a vagina of said patient while said electromyographic signals are being measured; and

diagnosing labor as a function of said signal analysis.

3. The method of claim 1, further comprising:

predicting treatment for said patient based on said characterization of uterine activity.

4. The method of claim 3, wherein said predicting step comprises pharmacologically inducing or inhibiting labor in said patient.

5. The method of claim 1, wherein said analyzing step further comprises isolating high frequency components (F2) within said electromyographic signals.

6. The method of claim 5, wherein said high frequency components (F2) are in the approximate range from 0.005 to 3.0 Hertz.

7. The method of claim 5, wherein said analyzing step further comprises:

isolating a fast wave component (FW) within said high frequency components (F2); and

determining a low-frequency (FW_L) domain, including low-frequency components within said fast wave component (FW), and a high-frequency (FW_H) domain, including high-frequency components within said fast wave component (FW).

8. The method of claim 7, wherein said low-frequency (FW_L) domain includes frequencies in the approximate range from 0.01 to 0.06 Hertz, and said high-frequency (FW_H) domain includes frequencies in the approximate range from 0.06 to 3.0 Hertz.

9. The method of claim 7, wherein said analyzing step further comprises determining a relationship between said low-frequency (FW_L) domain and said high-frequency (FW_H) domain indicative of an obstetrical diagnosis.

10. The method of claim 9, wherein said relationship is indicative of pre-term or term uterine activity.

11. The method of claim 7, wherein said analyzing step further comprises determining power density spectral characteristics of said frequency components of said electromyographic signals.

12. The method of claim 11, said analyzing step further comprises generating a 3-dimensional mesh plot of said power density spectral characteristics, said mesh plot displaying energy levels versus frequency versus time of pregnancy.

13. The method of claim 11, wherein said analyzing step further comprises:

creating a power density spectrum curve;

integrating said power density spectrum curved to determine an approximate total low energy for said low-frequency (FW_L) domain and an approximate total high energy for said high-frequency (FW_H) domain; and

determining a relationship between said approximate total low-energy and said approximate total high-energy indicative of an obstetrical diagnosis.

14. The method of claim 13, wherein said relationship is a ratio.

15. The method of claim 13, wherein said relationship is indicative of pre-term or term uterine activity.

16. The method of claim 1, wherein said analyzing step further comprises determining fast wavelet transform characteristics of said frequency components of bursts of action potentials within said electromyographic signals.

17. The method of claim 1, wherein said analyzing step further comprises determining joint time-frequency characteristics of said frequency components of bursts of action potentials within said electromyographic signals.

18. A method of analyzing surface electromyographic data to characterize uterine activity, comprising:

applying a plurality of action potential measuring electrodes to a surface of a patient;

measuring electromyographic signals produced by said electrodes;

analyzing said electromyographic signals

determining potential vector characteristics of said electromyographic signals to identify a direction of propagation of uterine electrical activity; and

characterizing uterine activity of said patient based on said potential vector characteristics.

19. The method of claim 18, wherein said analyzing step further comprises determining a uterine potential vector indicative of a obstetrical diagnosis.

20. The method of claim 19, wherein said diagnosis is of pre-term or term uterine activity.

21. A method of analyzing surface electromyographic data to characterize uterine activity, comprising:

applying action potential measuring electrodes to a surface of a patient;

measuring electromyographic signals produced by said electrodes;

analyzing said electromyographic signals;

integrating energy corresponding to bursts of action potentials within said electromyographic signals to determine an approximate total energy of said bursts of action potentials, and

characterizing uterine activity of said patient based on said approximate total energy.

22. The method of claim 21, wherein said analyzing step further comprises utilizing said approximate total energy and an approximate time for said bursts of action potentials to determine an approximate energy per unit of time, and wherein said characterizing step further comprises characterizing uterine activity of said patient based on said approximate energy per unit of time.

23. An apparatus for recording and analyzing uterine electrical activity from the abdominal surface, comprising:

at least one action potential measuring electrode applicable to a surface of a patient under analysis;

an analog-to-digital converter, connected to said at least one electrode, for converting electromyographic signals produced by said electrode into digitized data indicative of said electromyographic signals;

a memory for storing said digitized signals; and

a programmed computer for analyzing frequency components of said stored digitized electromyographic signals, and for providing an indication of uterine electrical activity of said patient under analysis as a function of said stored digitized signals.

24. The apparatus of claim 23, wherein said programmed computer is further for isolating a fast wave component (FW) within said stored digitized electromyographic signals, for determining a low-frequency (FW_L) domain, including low-frequency components within said fast wave component (FW), and for determining a high-frequency (FW_H) domain, including high-frequency components within said fast wave component (FW).

25. The apparatus of claim 24, wherein said programmed computer is further for determining a relationship

between said low-frequency (FW_L) domain and said high-frequency (FW_H) domain indicative of an obstetrical diagnosis.

26. The apparatus of claim 23, wherein said programmed computer is further for determining power density spectral characteristics of said frequency components of said electromyographic signals.

27. The apparatus of claim 23, wherein said programmed computer is further for creating a power density spectrum curve, for integrating said power density spectrum curved to determine an approximate total low energy for said low-frequency (FW_L) domain and an approximate total high energy for said high-frequency (FW_H) domain, and for determining a relationship between said approximate total low-energy and said approximate total high-energy indicative of an obstetrical diagnosis.

28. An apparatus for recording and analyzing uterine electrical activity from the abdominal surface, comprising:

a plurality of action potential measuring electrodes applicable to a surface of a patient under analysis;

an analog-to-digital converter, connected to said plurality of electrodes, for converting electromyographic signals produced by said electrodes into digitized data indicative of said electromyographic signals;

a memory for storing said digitized signals; and

a programmed computer for analyzing said stored digitized electromyographic signals, for determining potential vector characteristics of said electromyographic signals to identify a direction of propagation of uterine electrical activity, and for providing an indication of uterine electrical activity of said patient under analysis as a function of said potential vector characteristics.

29. A remote uterine monitoring system for analyzing surface electromyographic data to characterize uterine activity, comprising:

a remote uterine monitor including:

at least one action potential measuring electrode applicable to a surface of a patient under analysis; and

a remote analog-to-digital converter, connected to said at least one electrode, for converting electromyographic signals produced by said electrode into digitized data indicative of said electromyographic signals; and

a central programmed computer in communication with said remote uterine monitor for analyzing said stored digitized electromyographic signals, and for providing an indication of uterine electrical activity of said patient under analysis as a function of said stored digitized signals.

30. The remote uterine monitoring system of claim 29, wherein said remote uterine monitor and said central programmed computer communicate on-line through a telephone line.

31. The remote uterine monitoring system of claim 29, further comprising a remote storage device for recording said digitized electromyographic signal data, and wherein said central programmed computer communicates with said remote uterine monitor off-line utilizing said remote storage device.

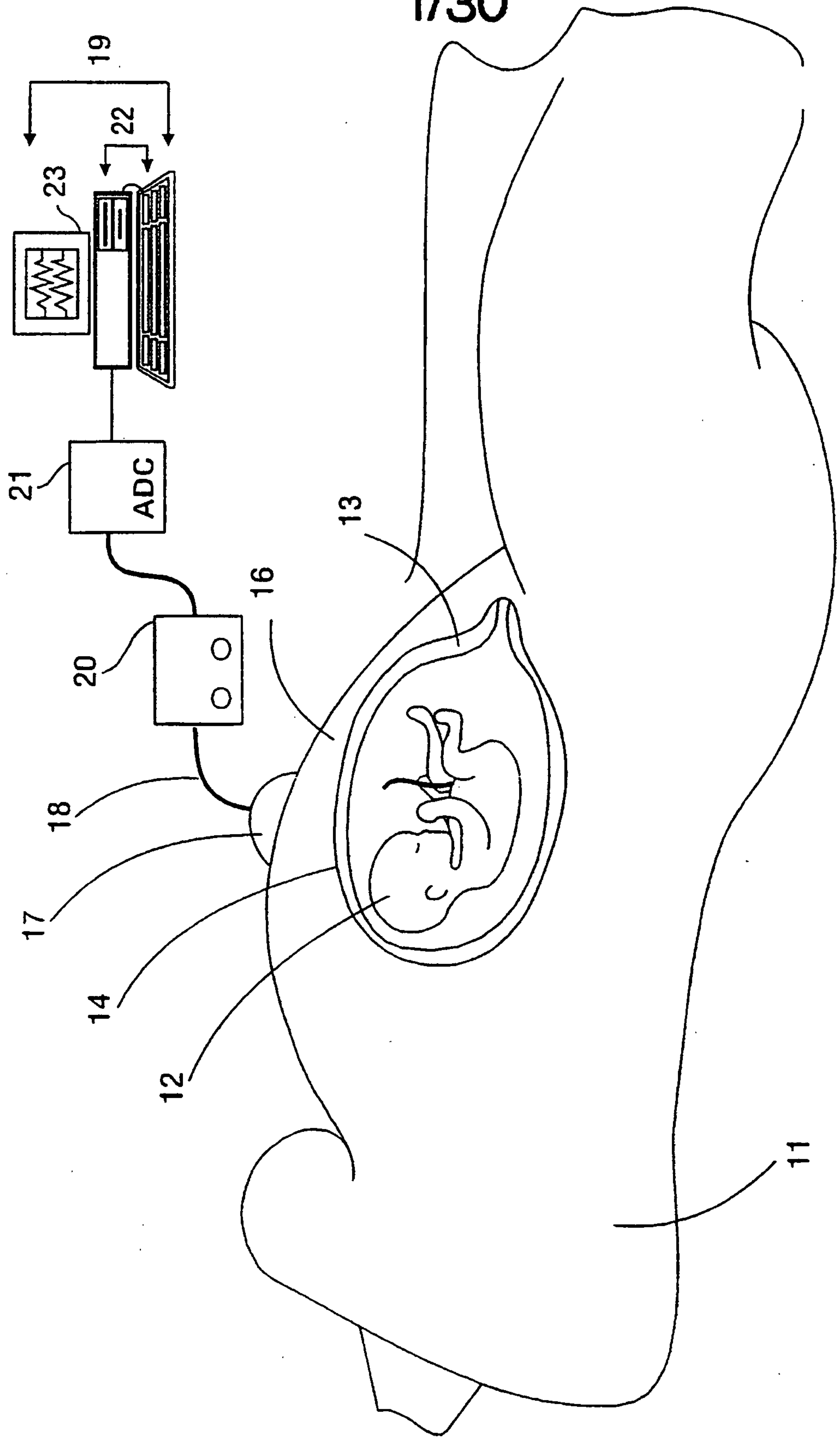


FIG. 1

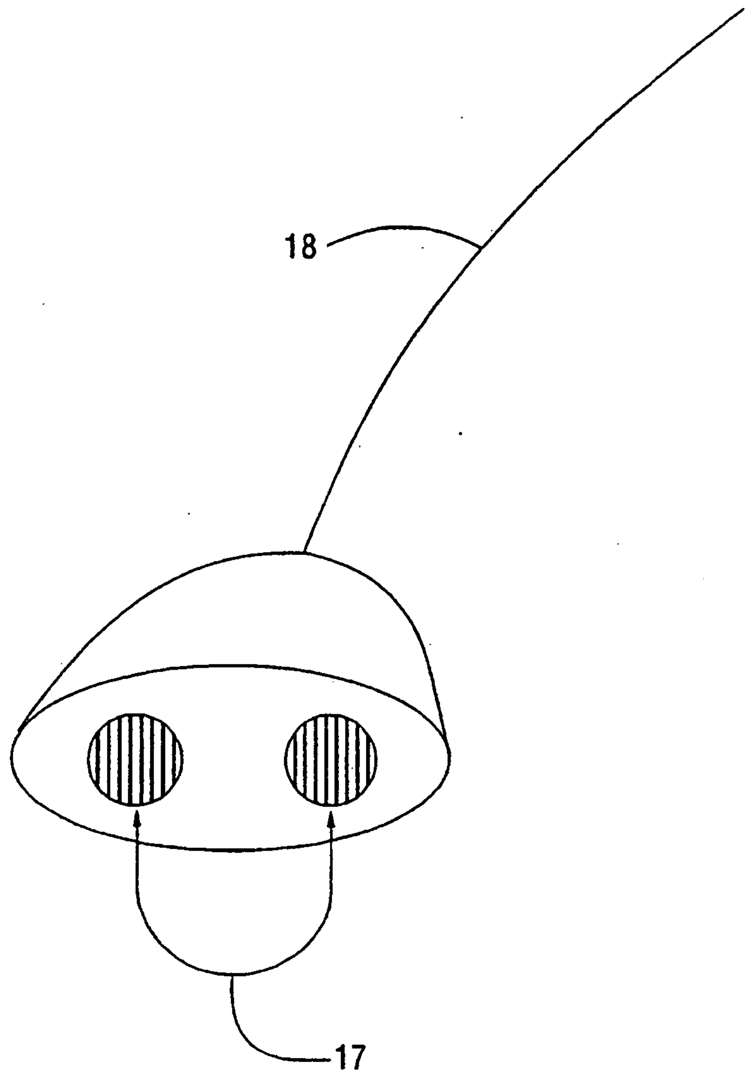


FIG. 2

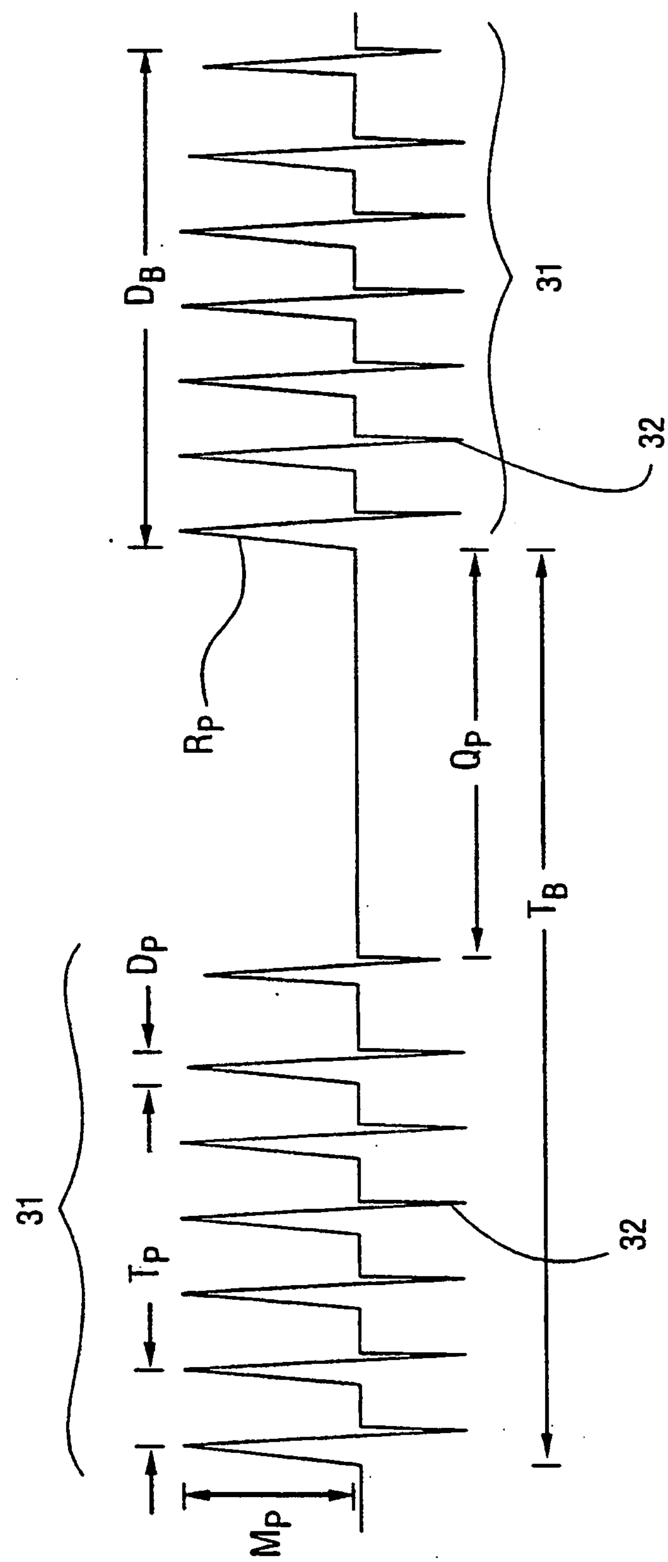


FIG. 3

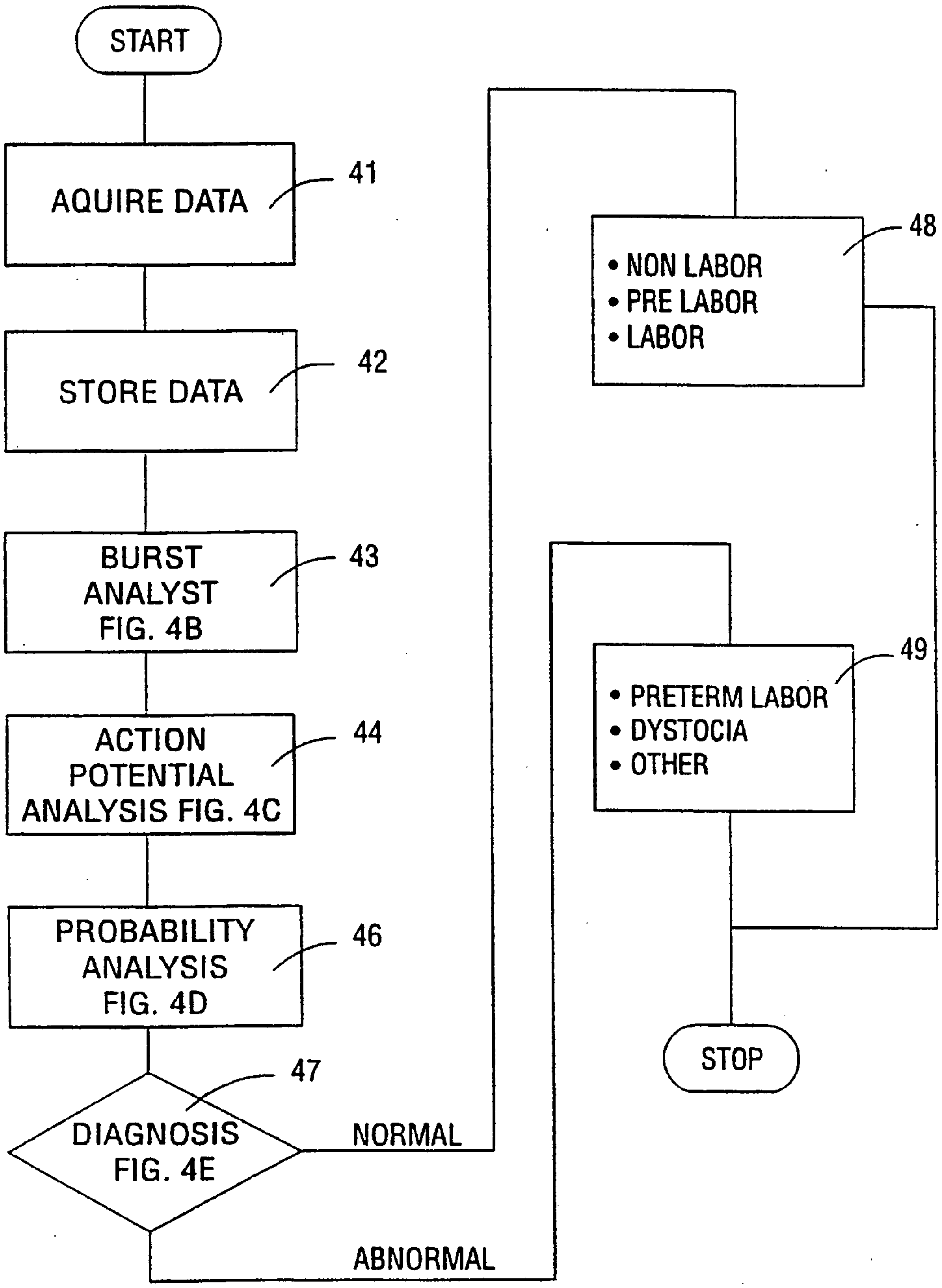

START
AQUIRE DATA
41
STORE DATA
42
BURST ANALYST FIG. 4B
43
ACTION POTENTIAL ANALYSIS FIG. 4C
44
PROBABILITY ANALYSIS FIG. 4D
46
DIAGNOSIS FIG. 4E
47
NORMAL
ABNORMAL
• NON LABOR
• PRE LABOR
• LABOR
48
• PRETERM LABOR
• DYSTOCIA
• OTHER
49
STOP

FIG. 4A

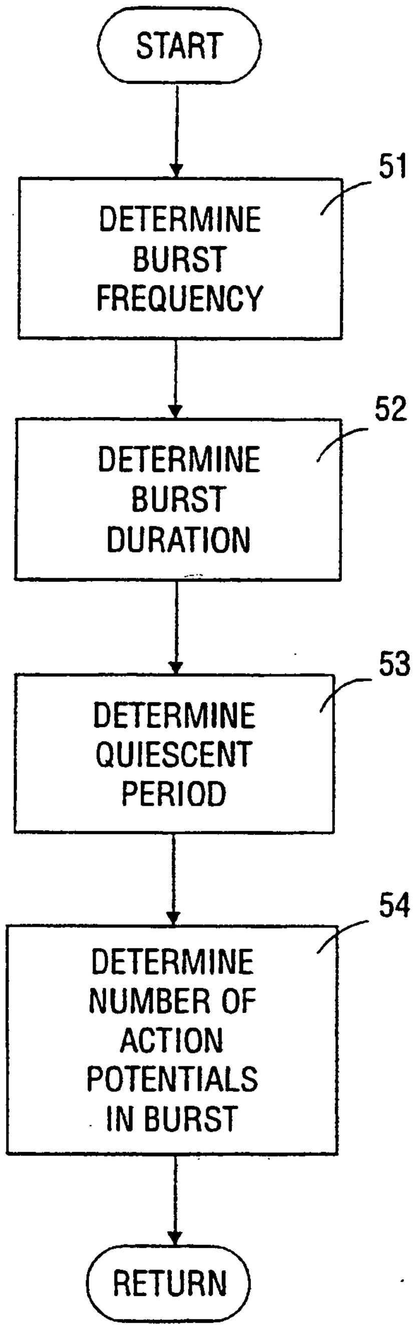

START
51
DETERMINE BURST FREQUENCY
52
DETERMINE BURST DURATION
53
DETERMINE QUIESCENT PERIOD
54
DETERMINE NUMBER OF ACTION POTENTIALS IN BURST
RETURN

FIG. 4B

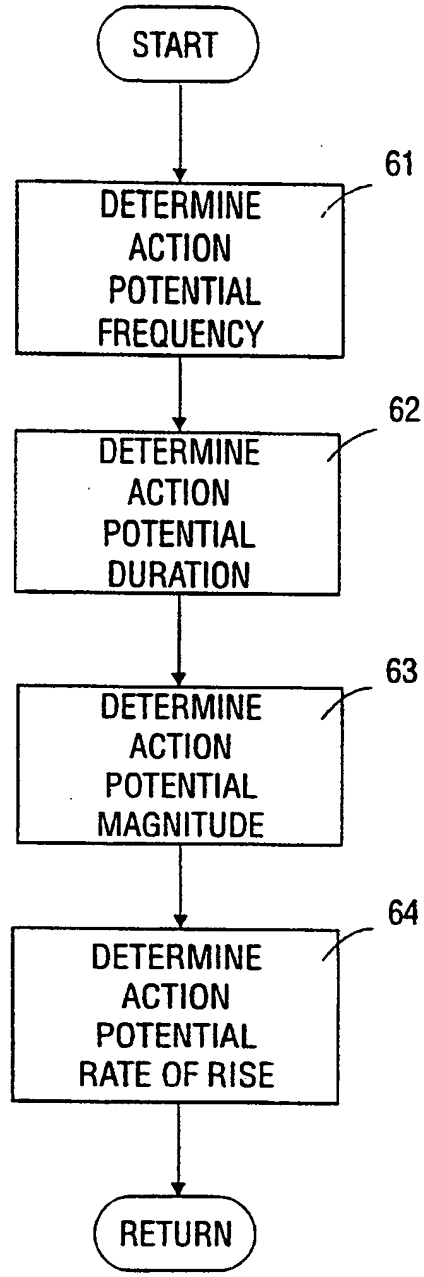

START
61
DETERMINE ACTION POTENTIAL FREQUENCY
62
DETERMINE ACTION POTENTIAL DURATION
63
DETERMINE ACTION POTENTIAL MAGNITUDE
64
DETERMINE ACTION POTENTIAL RATE OF RISE
RETURN

FIG. 4C

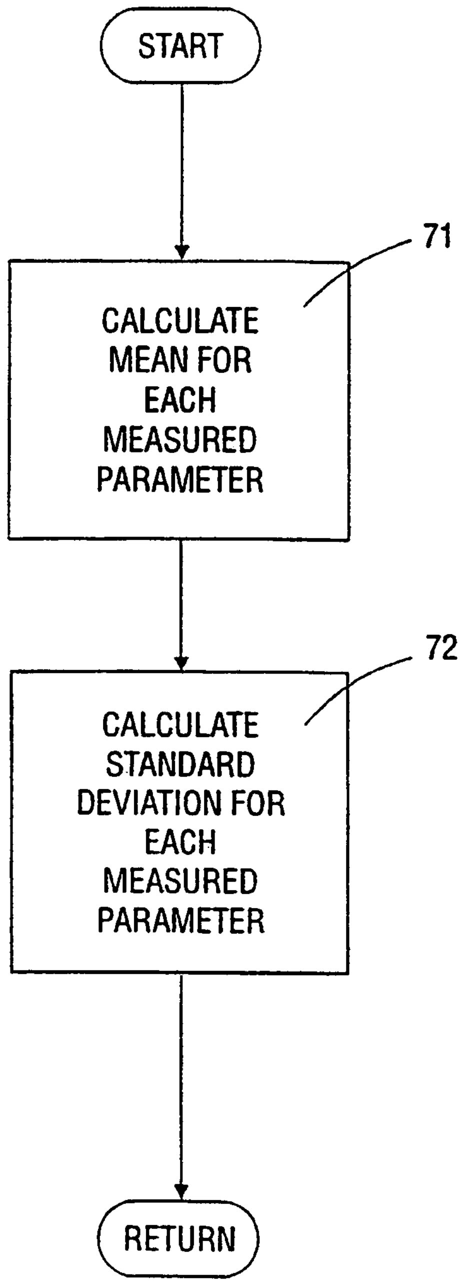

START
71
CALCULATE MEAN FOR EACH MEASURED PARAMETER
72
CALCULATE STANDARD DEVIATION FOR EACH MEASURED PARAMETER
RETURN

FIG. 4D

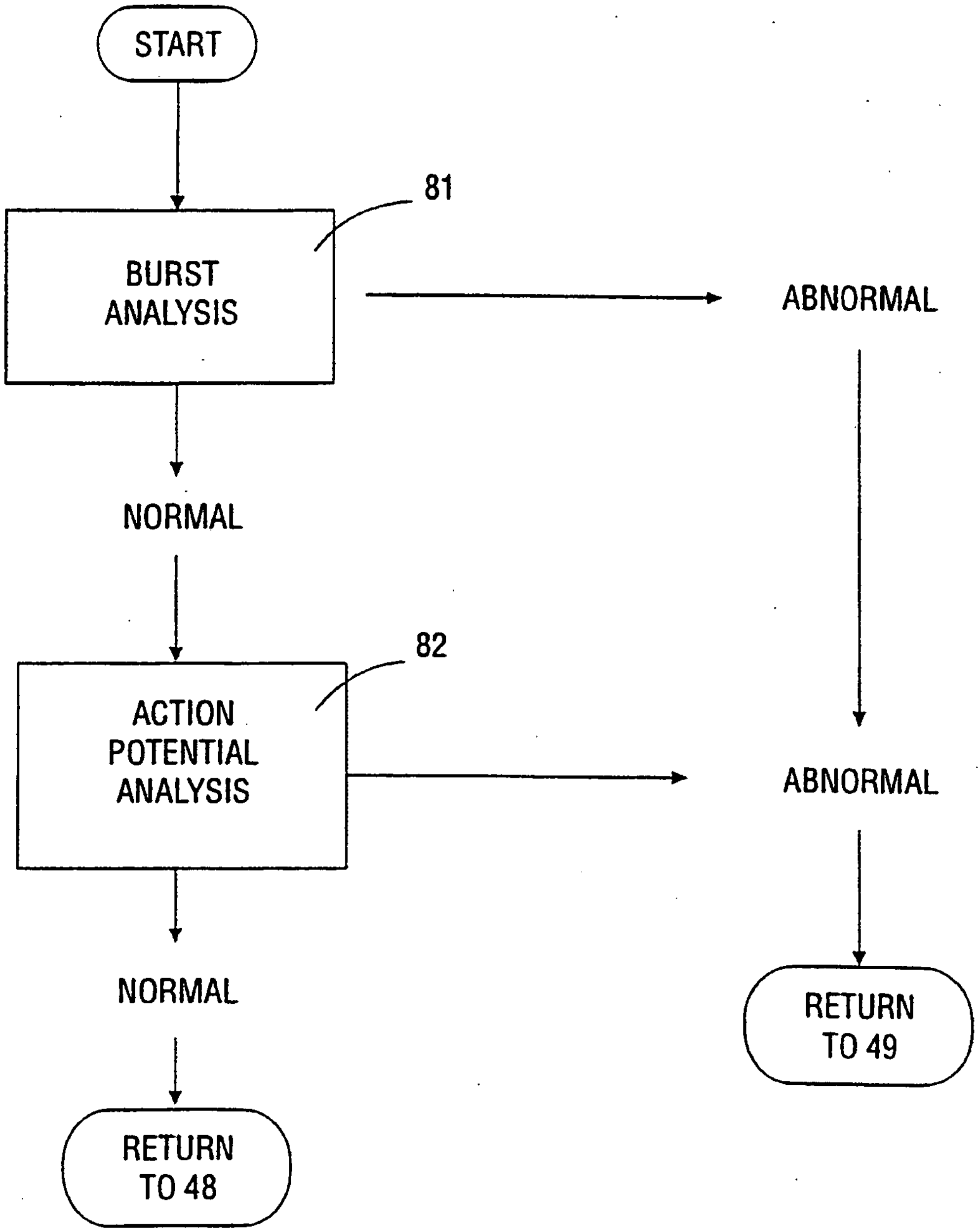
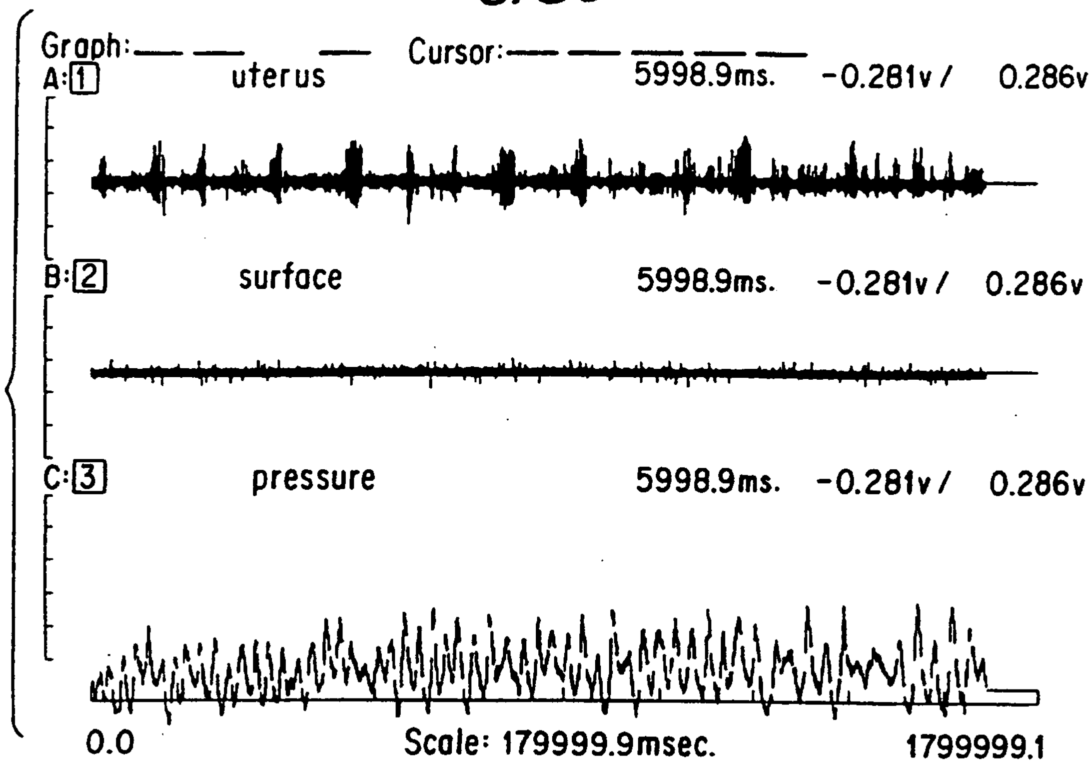
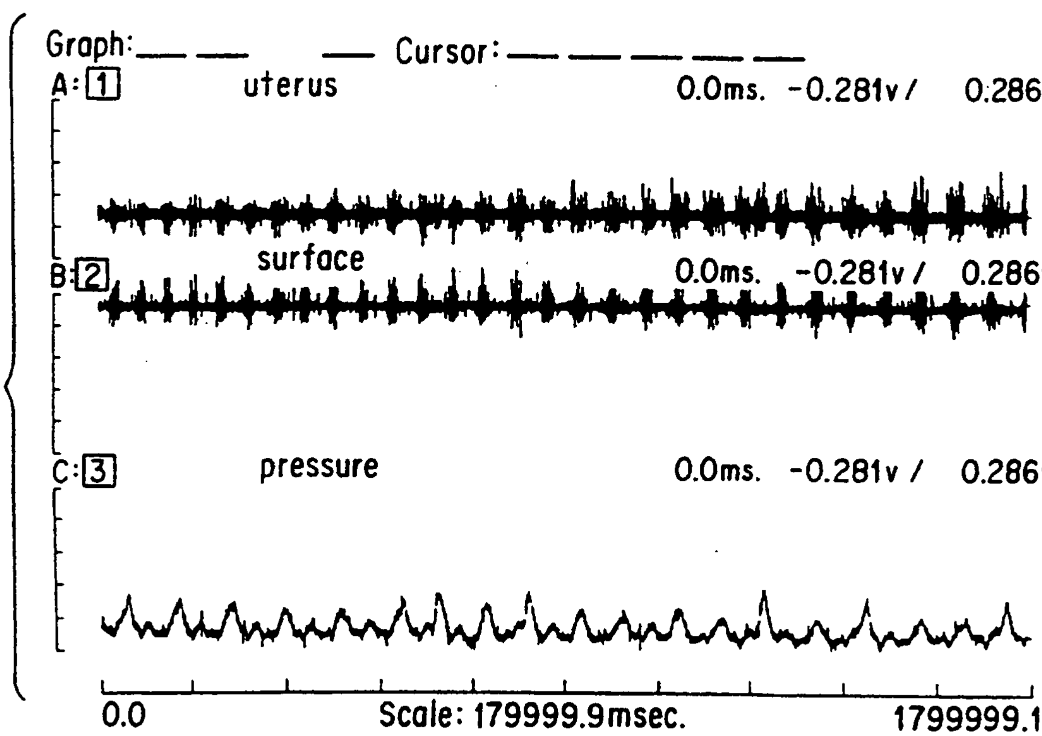

START
81
BURST ANALYSIS
ABNORMAL
NORMAL
82
ACTION POTENTIAL ANALYSIS
ABNORMAL
NORMAL
RETURN TO 49
RETURN TO 48

FIG. 4E



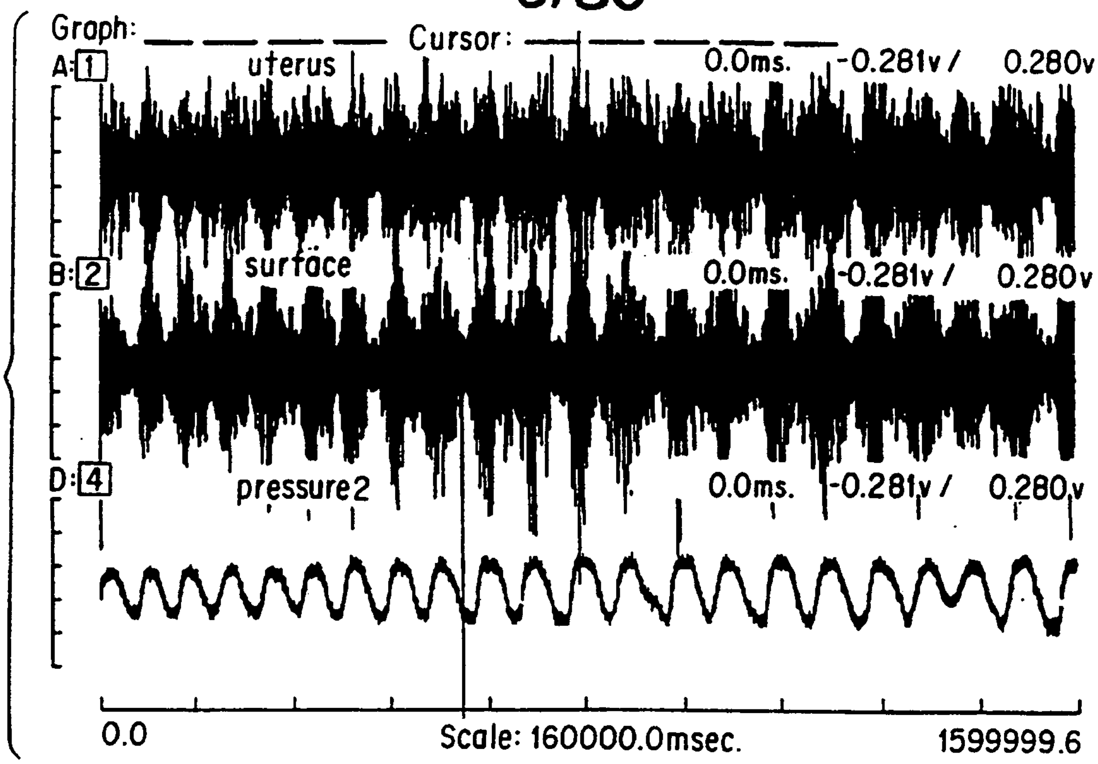
Graph:
Cursor:
A: 1 uterus 5998.9ms. -0.281v / 0.286v
B: 2 surface 5998.9ms. -0.281v / 0.286v
C: 3 pressure 5998.9ms. -0.281v / 0.286v
0.0
Scale: 179999.9msec.
1799999.1

FIG. 5



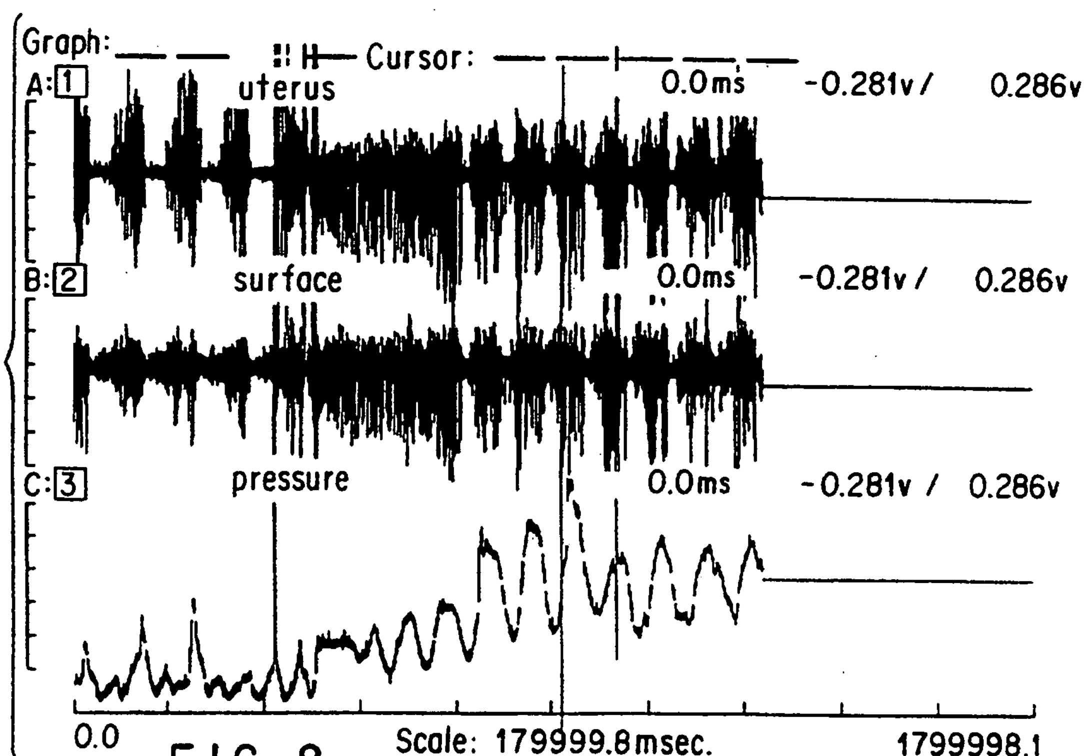
Graph:
Cursor:
A: 1 uterus 0.0ms. -0.281v / 0.286v
B: 2 surface 0.0ms. -0.281v / 0.286v
C: 3 pressure 0.0ms. -0.281v / 0.286v
0.0
Scale: 179999.9msec.
1799999.1

FIG. 6



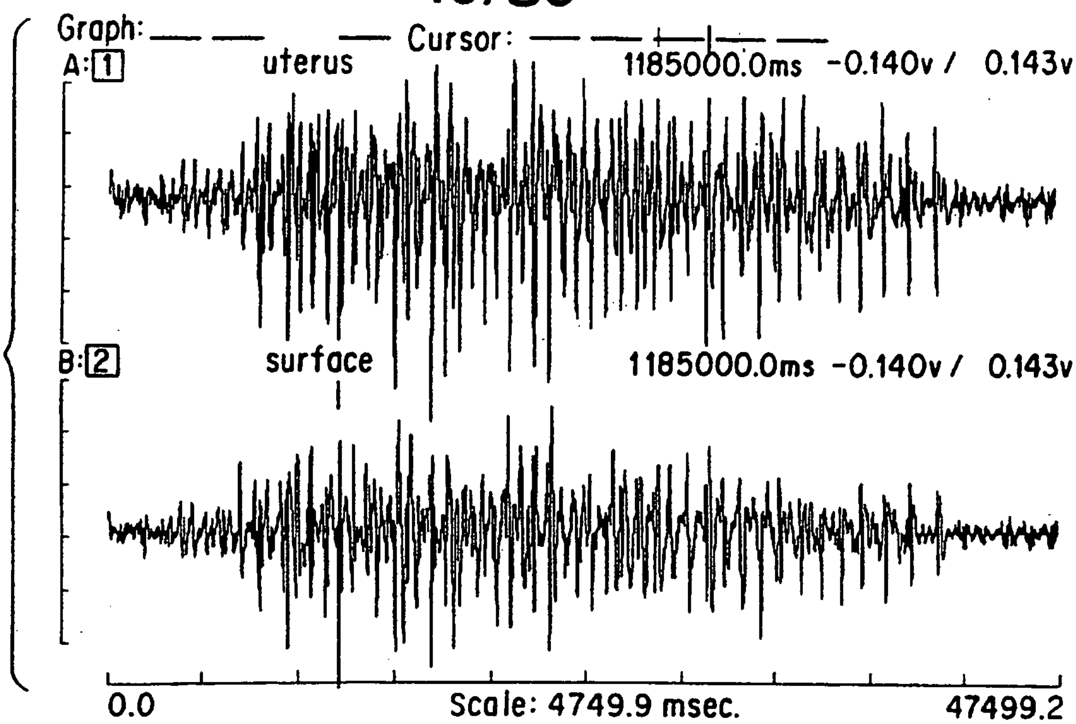
Graph:
Cursor:
A: 1 uterus 0.0ms. -0.281v / 0.280v
B: 2 surface 0.0ms. -0.281v / 0.280v
D: 4 pressure2 0.0ms. -0.281v / 0.280v
0.0
Scale: 160000.0msec.
1599999.6

FIG. 7



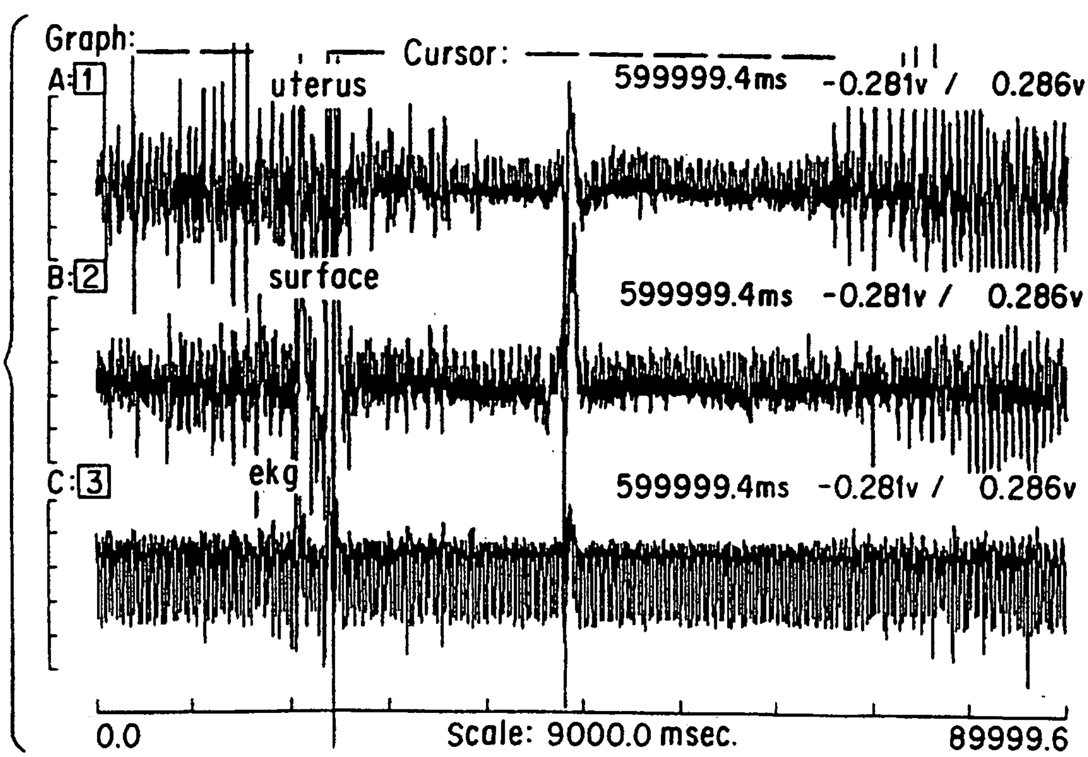
Graph:
Cursor:
A: 1 uterus 0.0ms -0.281v / 0.286v
B: 2 surface 0.0ms -0.281v / 0.286v
C: 3 pressure 0.0ms -0.281v / 0.286v
0.0
Scale: 179999.8msec.
1799998.1

FIG. 8



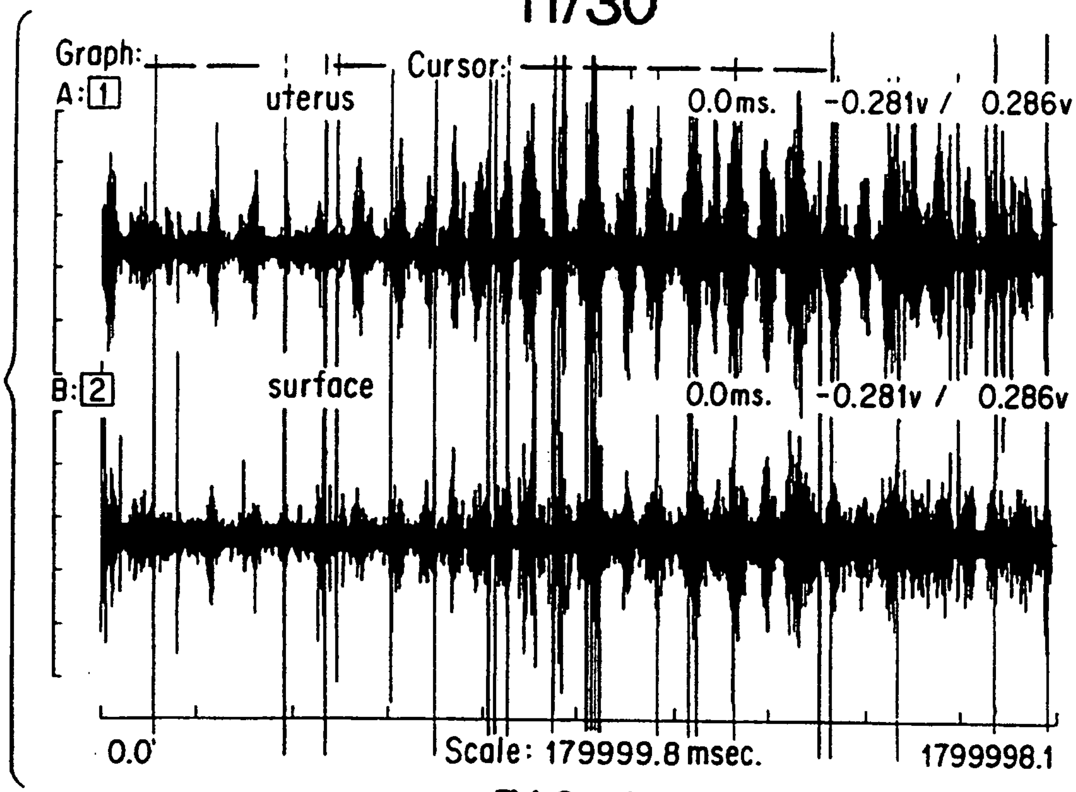
Graph:
Cursor:
A: 1 uterus
1185000.0ms -0.140v / 0.143v
B: 2 surface
1185000.0ms -0.140v / 0.143v
0.0
Scale: 4749.9 msec.
47499.2

FIG. 9



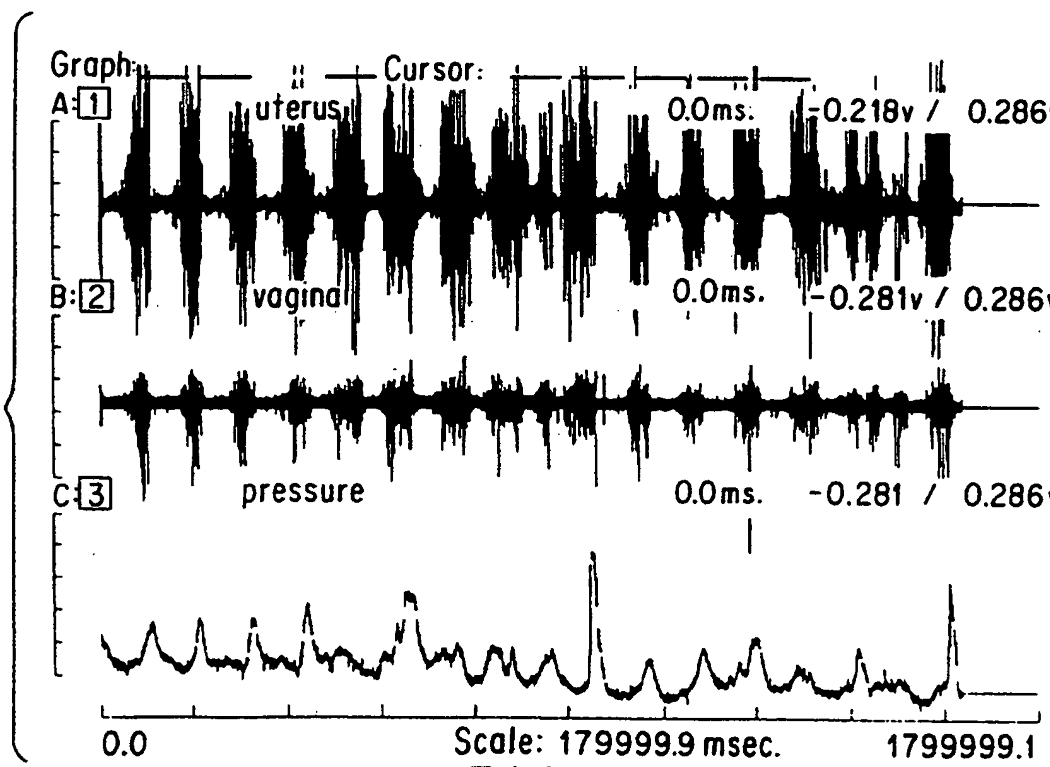
Graph:
Cursor:
A: 1 uterus
599999.4ms -0.281v / 0.286v
B: 2 surface
599999.4ms -0.281v / 0.286v
C: 3 ekg
599999.4ms -0.281v / 0.286v
0.0
Scale: 9000.0 msec.
89999.6

FIG. 10



Graph:
Cursor:
A: 1
uterus
0.0ms.
-0.281v / 0.286v
B: 2
surface
0.0ms.
-0.281v / 0.286v
0.0
Scale: 179999.8 msec.
1799998.1

FIG. 11



Graph
Cursor:
A: 1
uterus
0.0ms.
-0.218v / 0.286v
B: 2
vagina
0.0ms.
-0.281v / 0.286v
C: 3
pressure
0.0ms.
-0.281 / 0.286v
0.0
Scale: 179999.9 msec.
1799999.1

FIG. 12

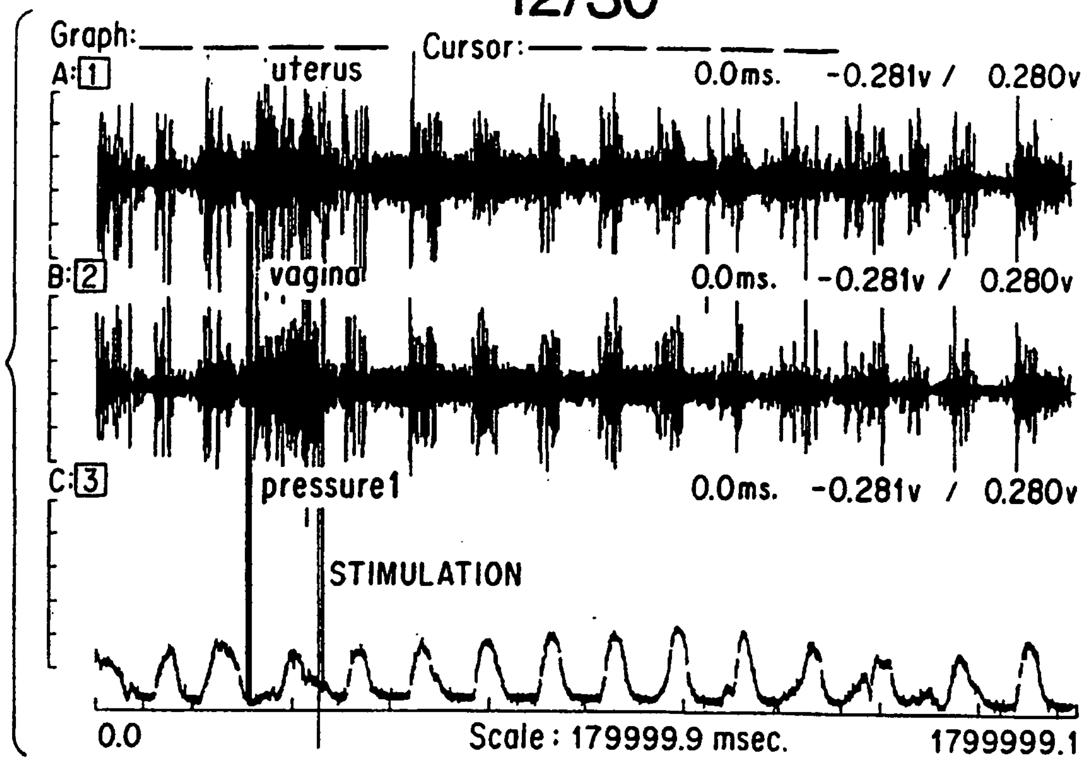

Graph:
Cursor:
A: 1 uterus
0.0ms. -0.281v / 0.280v
B: 2 vagina
0.0ms. -0.281v / 0.280v
C: 3 pressure1
0.0ms. -0.281v / 0.280v
STIMULATION
0.0
Scale: 179999.9 msec.
1799999.1

FIG. 13

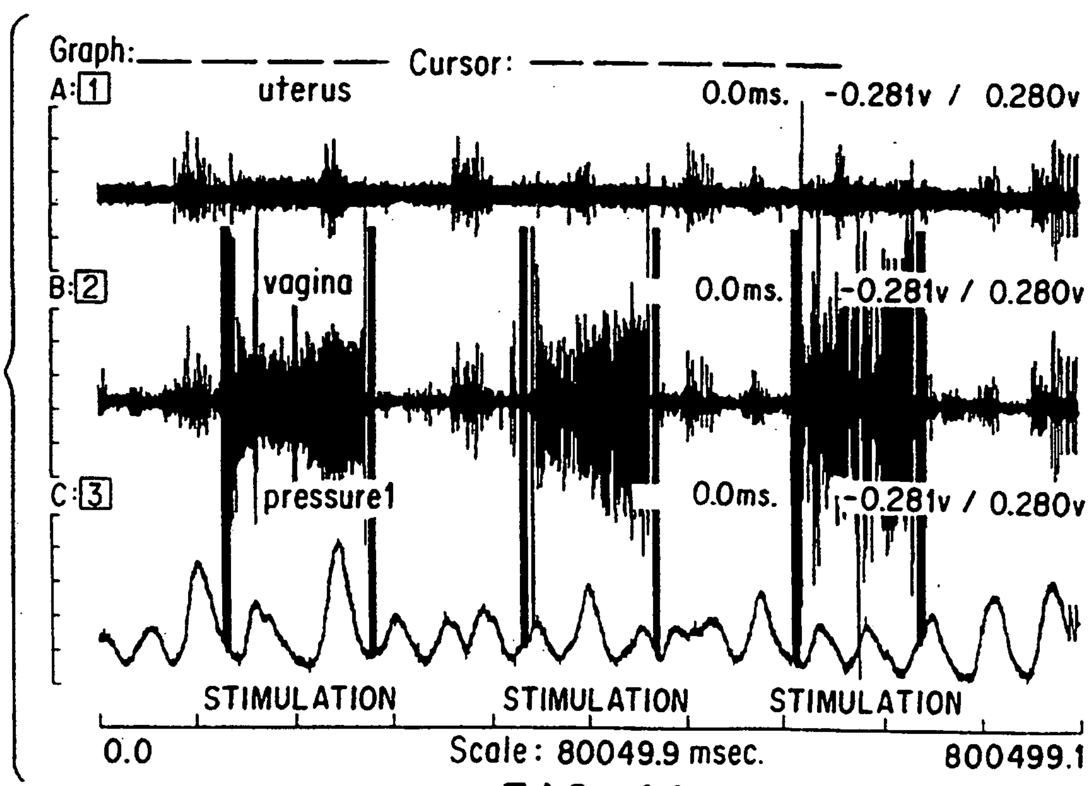

Graph:
Cursor:
A: 1 uterus
0.0ms. -0.281v / 0.280v
B: 2 vagina
0.0ms. -0.281v / 0.280v
C: 3 pressure1
0.0ms. -0.281v / 0.280v
STIMULATION
STIMULATION
STIMULATION
0.0
Scale: 80049.9 msec.
800499.1

FIG. 14

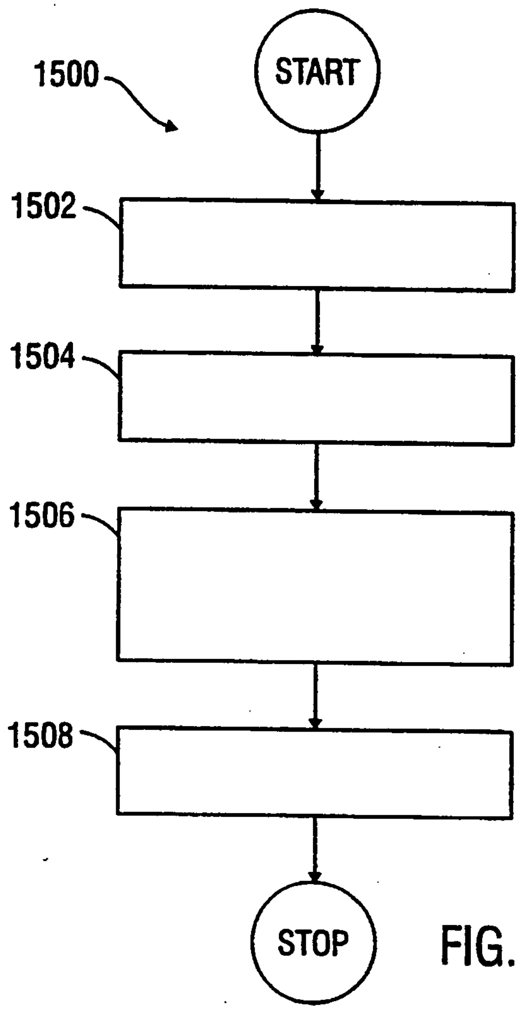

1500
START
1502
1504
1506
1508
STOP

FIG. 15

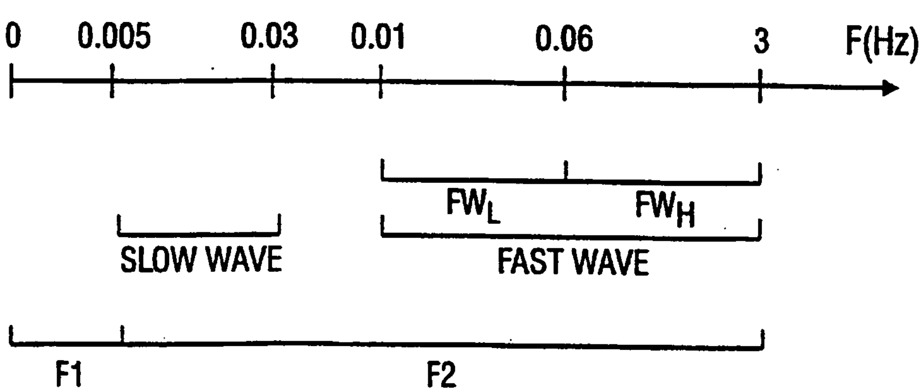

0
0.005
0.03
0.01
0.06
3
F(Hz)
FWL
FWH
SLOW WAVE
FAST WAVE
F1
F2

FIG. 16

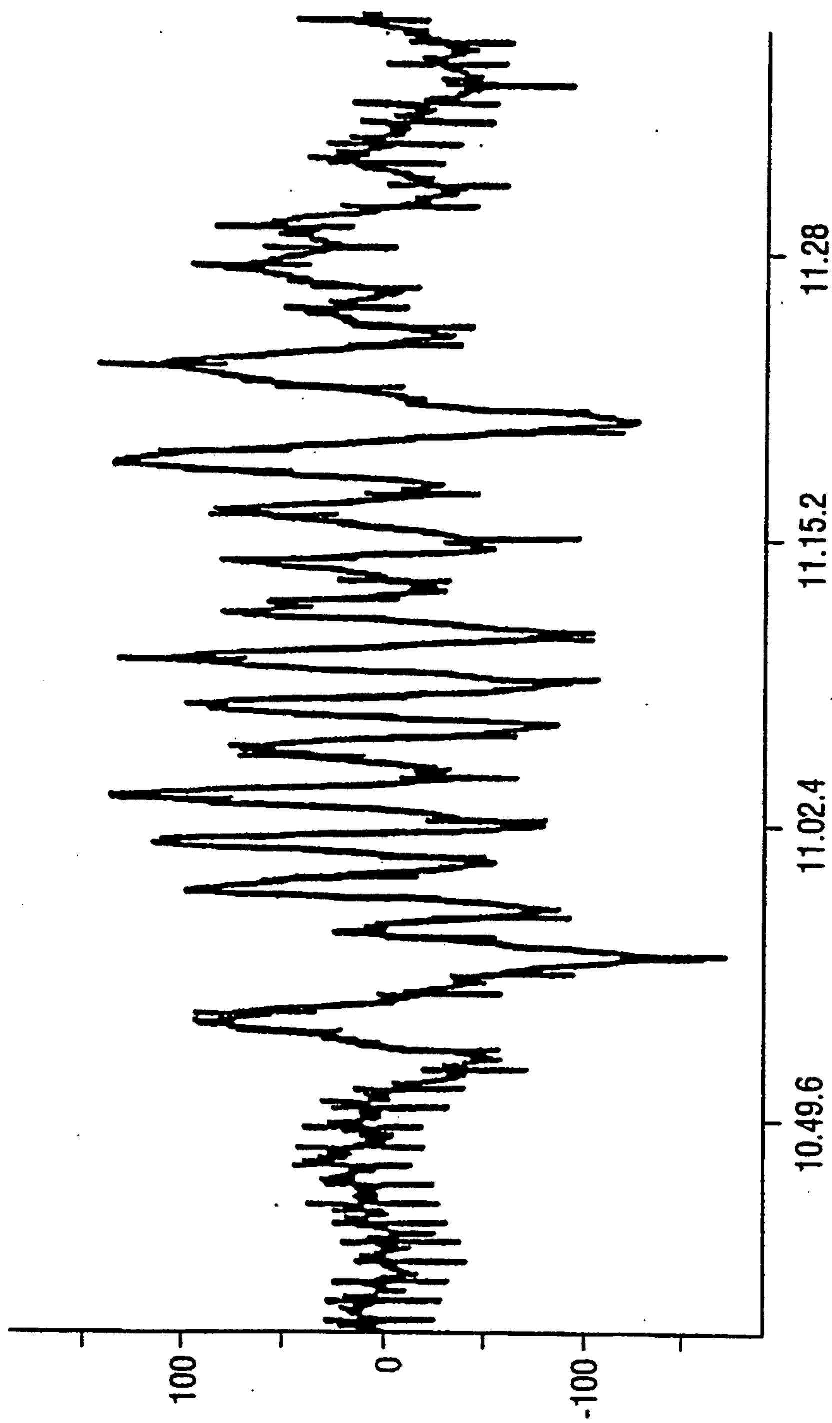


FIG. 17

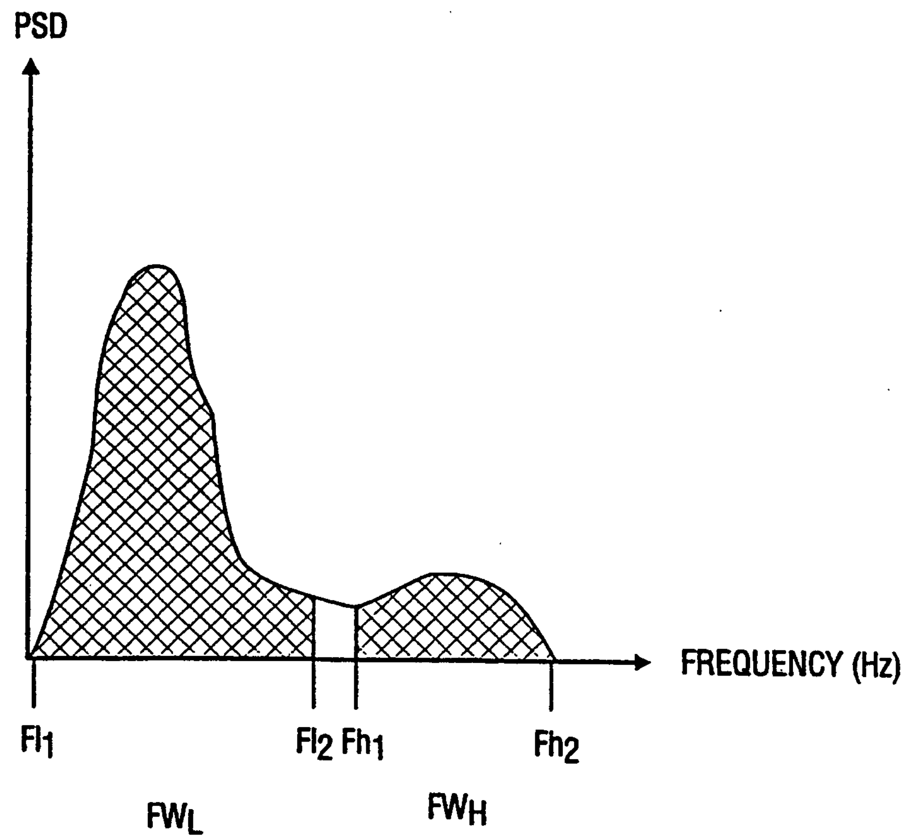


FIG. 18

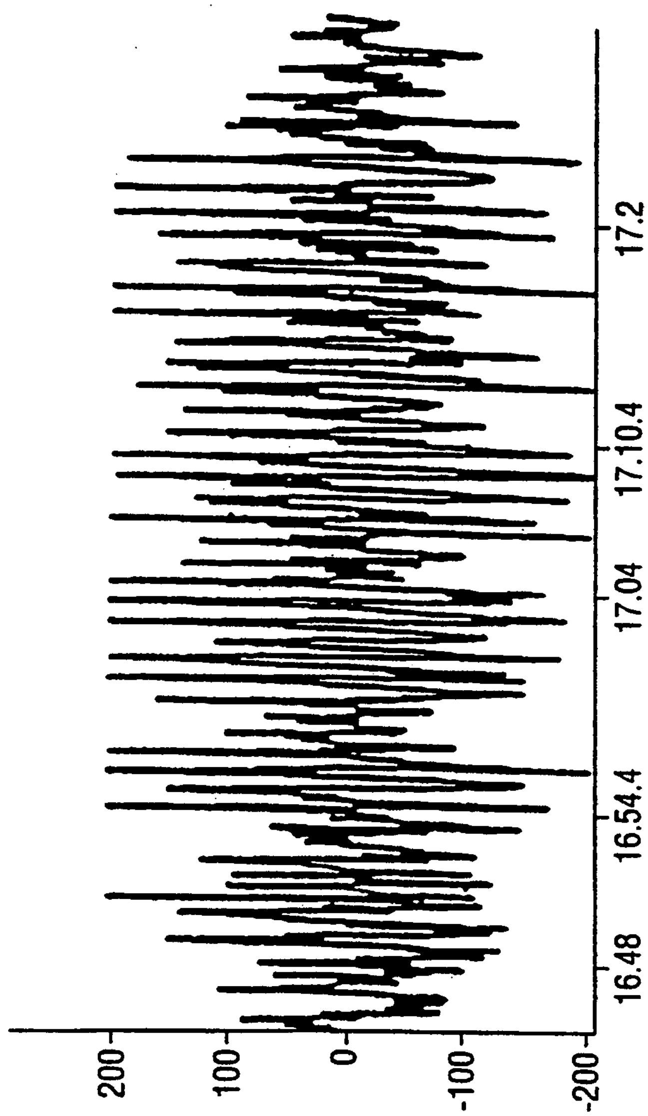


FIG. 19A

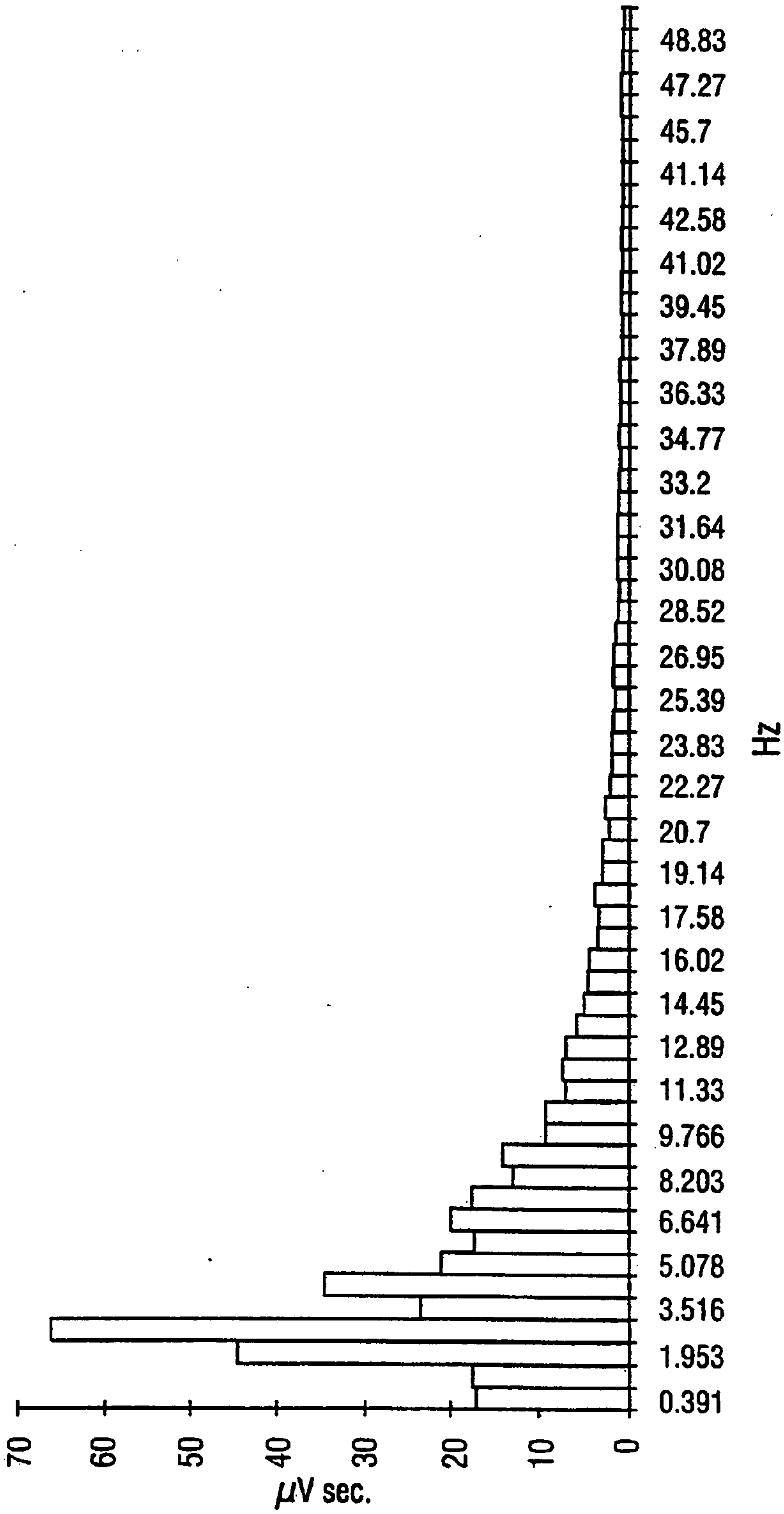

48.83
47.27
45.7
41.14
42.58
41.02
39.45
37.89
36.33
34.77
33.2
31.64
30.08
28.52
26.95
25.39
23.83
22.27
20.7
19.14
17.58
16.02
14.45
12.89
11.33
9.766
8.203
6.641
5.078
3.516
1.953
0.391
Hz
70
60
50
40
30
20
10
0
μV sec.

FIG. 19B

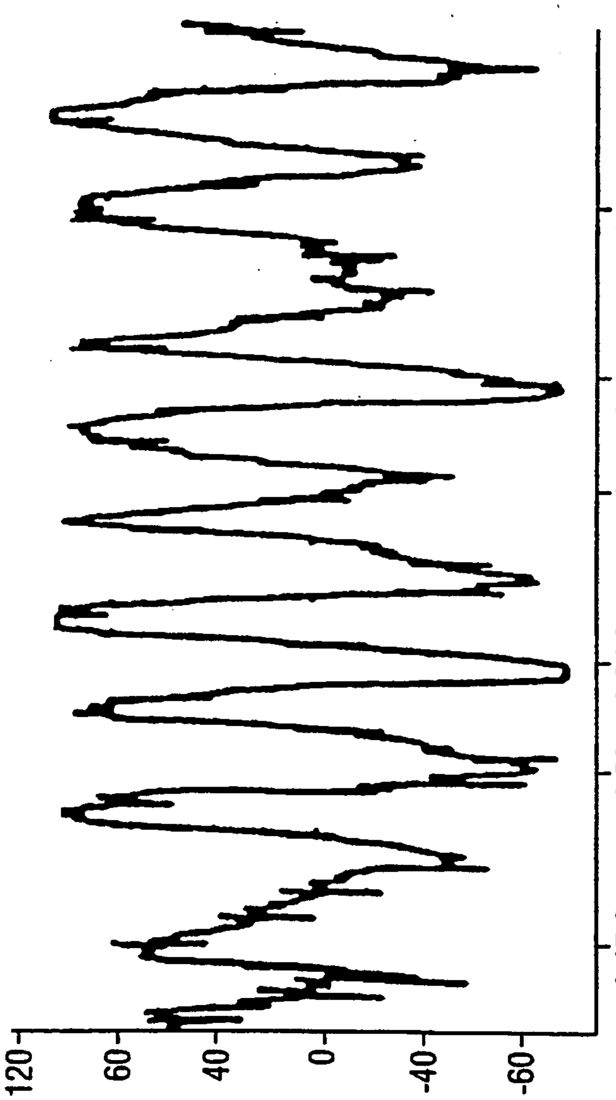
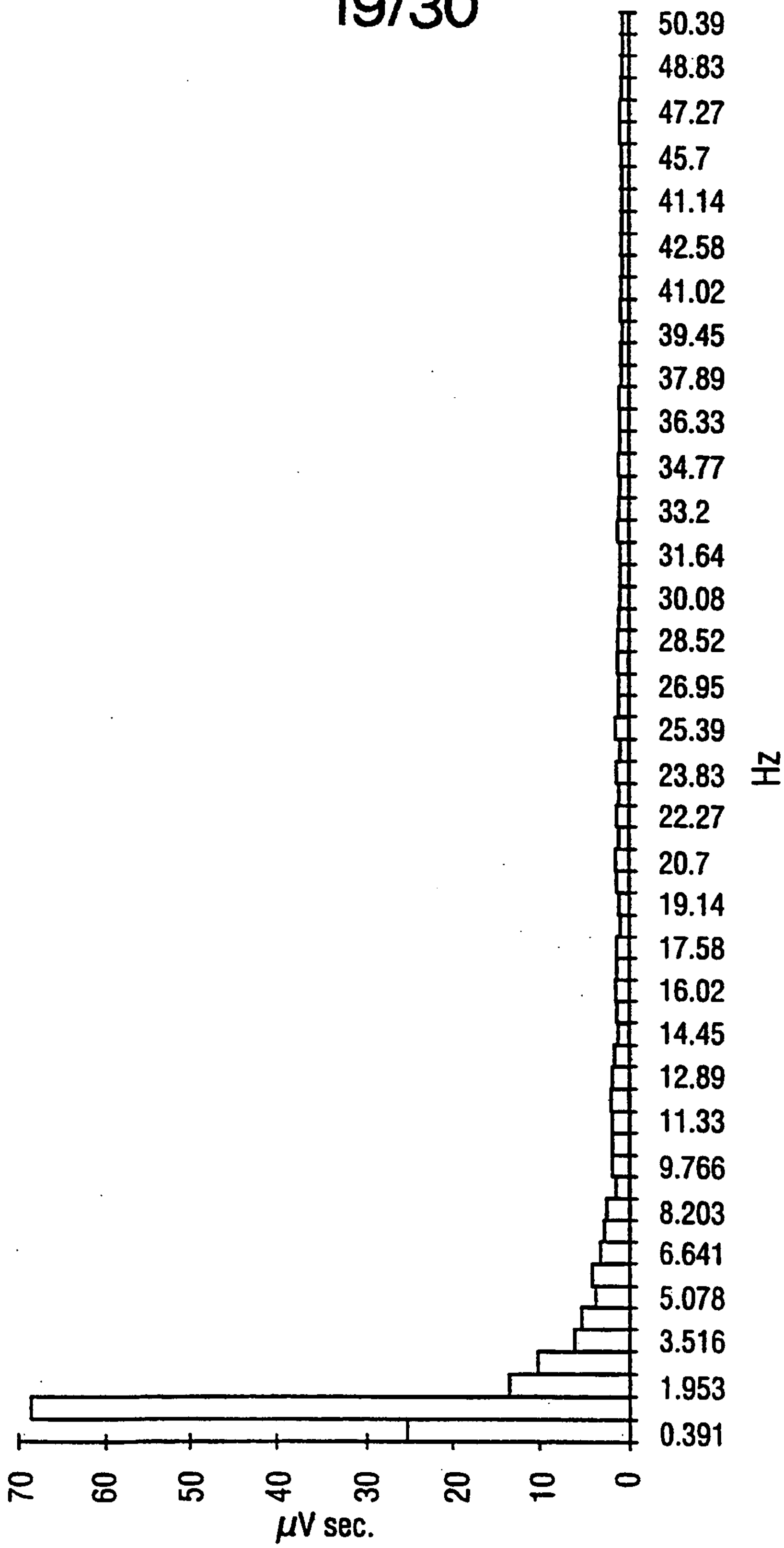


FIG. 20A



50.39
48.83
47.27
45.7
41.14
42.58
41.02
39.45
37.89
36.33
34.77
33.2
31.64
30.08
28.52
26.95
25.39
23.83
22.27
20.7
19.14
17.58
16.02
14.45
12.89
11.33
9.766
8.203
6.641
5.078
3.516
1.953
0.391
Hz
70
60
50
40
30
20
10
0
μV sec.

FIG. 20B

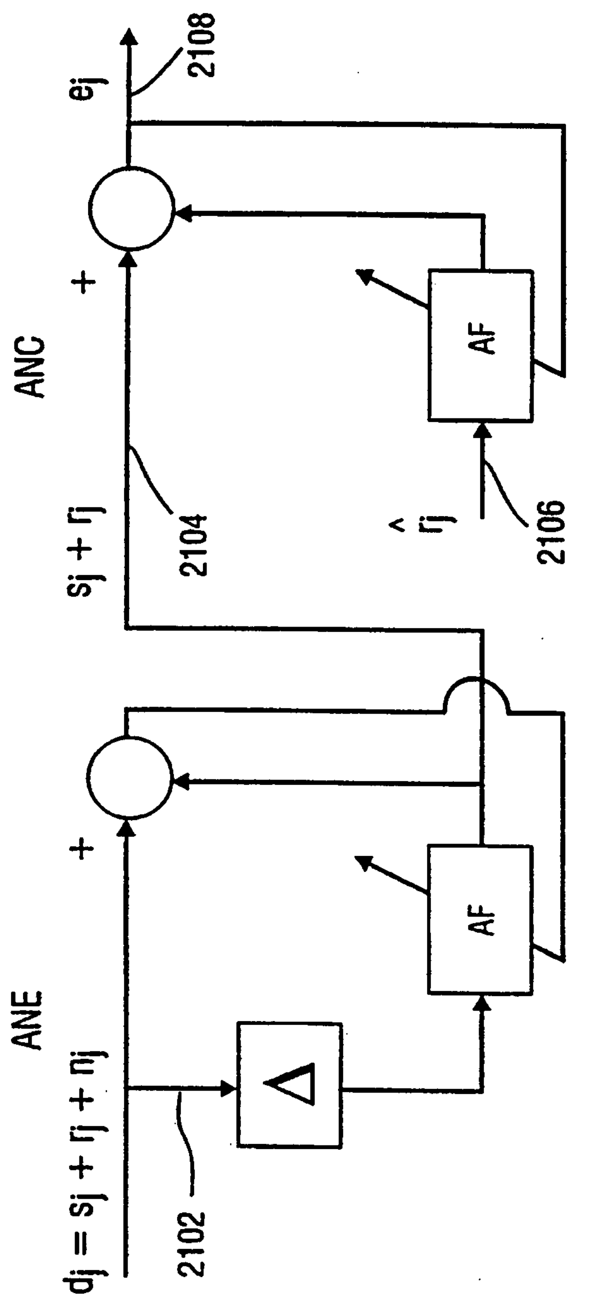


FIG. 21

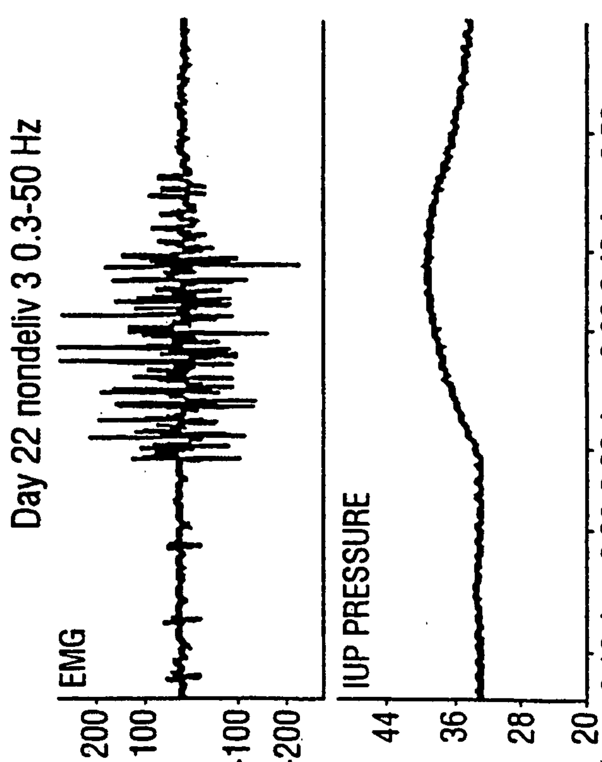


FIG. 22A

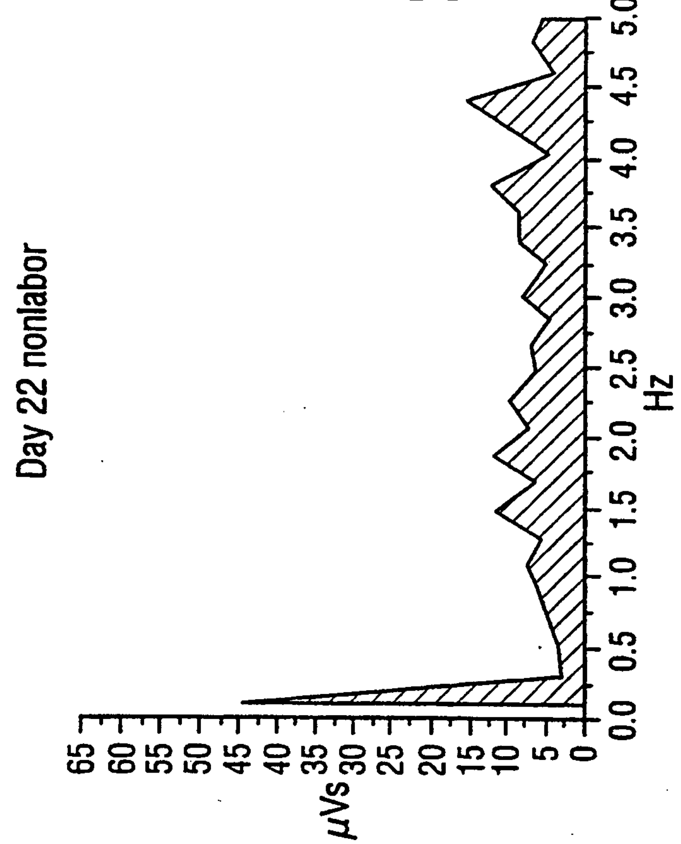


FIG. 22B

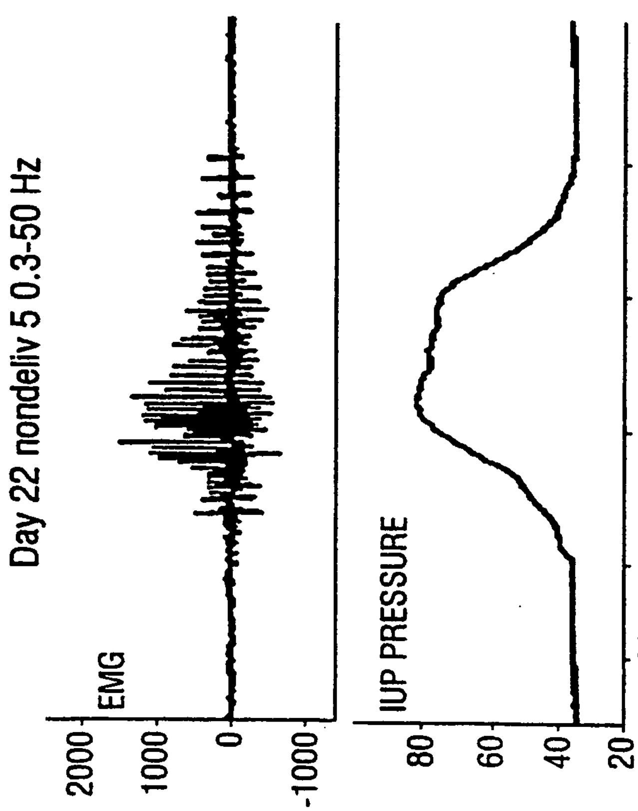


FIG. 22C

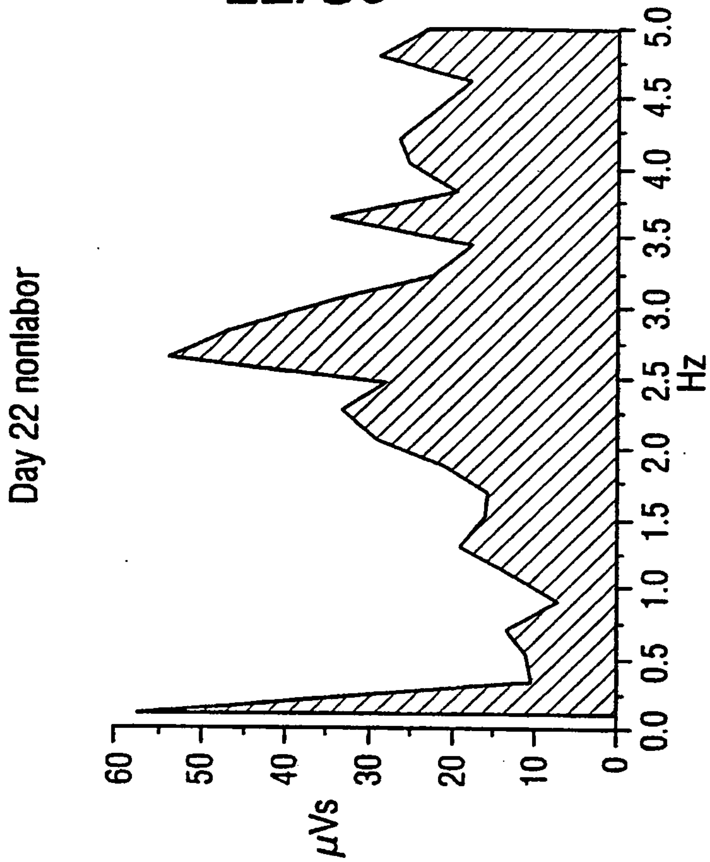


FIG. 22D

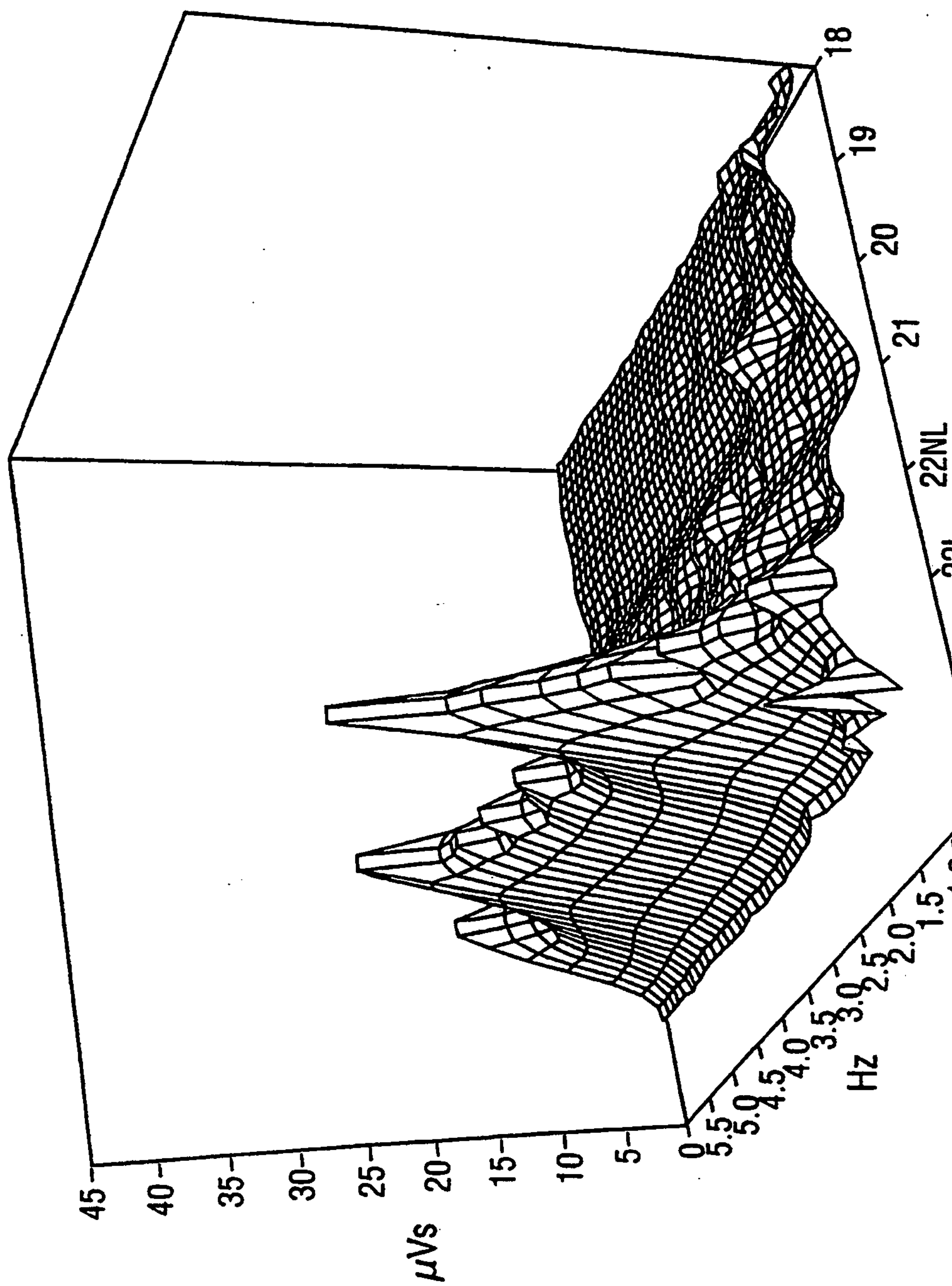
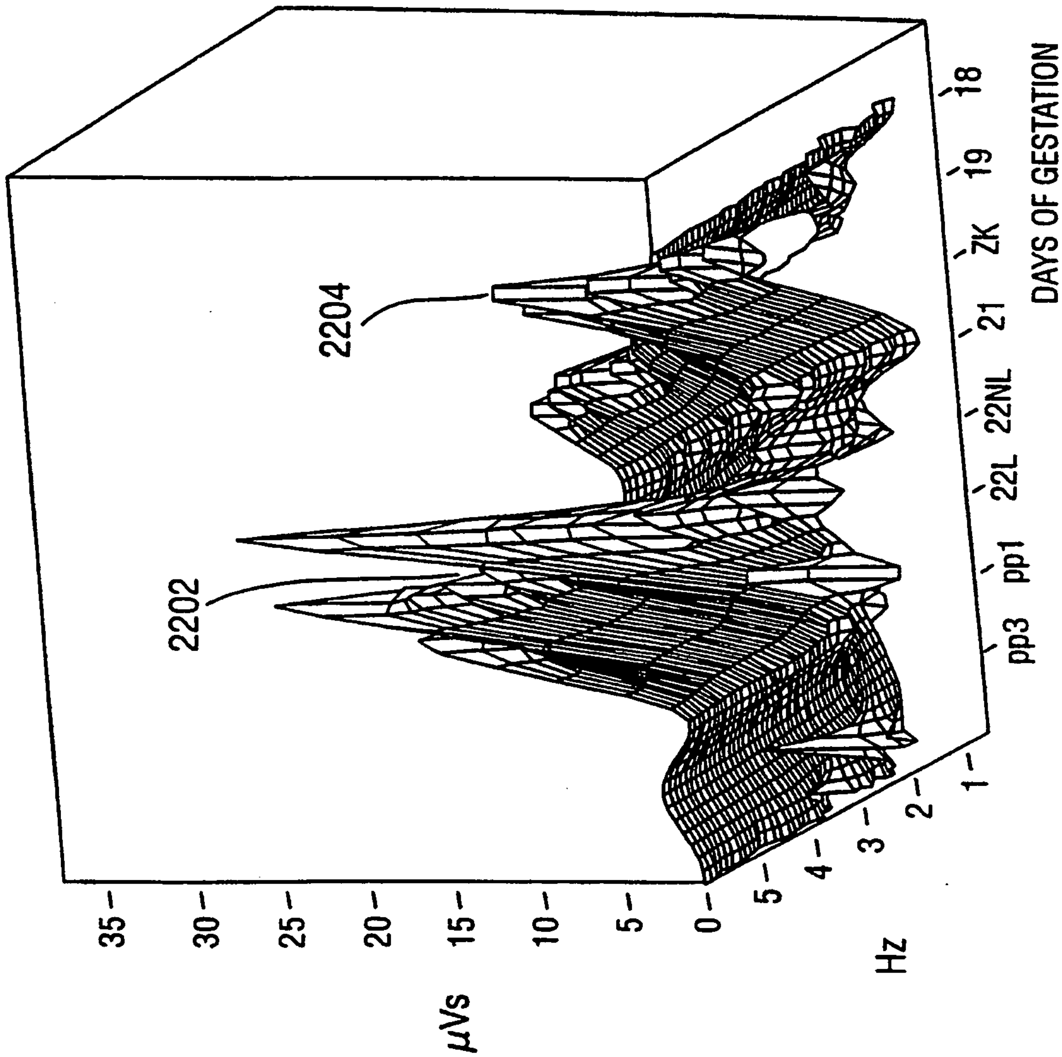

μVs
45
40
35
30
25
20
15
10
5
0
Hz
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
DAYS OF GESTATION
18
19
20
21
22NL
22L
pp1
pp2

FIG. 22E

FIG. 22F


2202
2204
35
30
25
20
15
10
5
0
μVs
Hz
5
4
3
2
1
pp3
pp1
22L
22NL
21
ZK
19
18
DAYS OF GESTATION

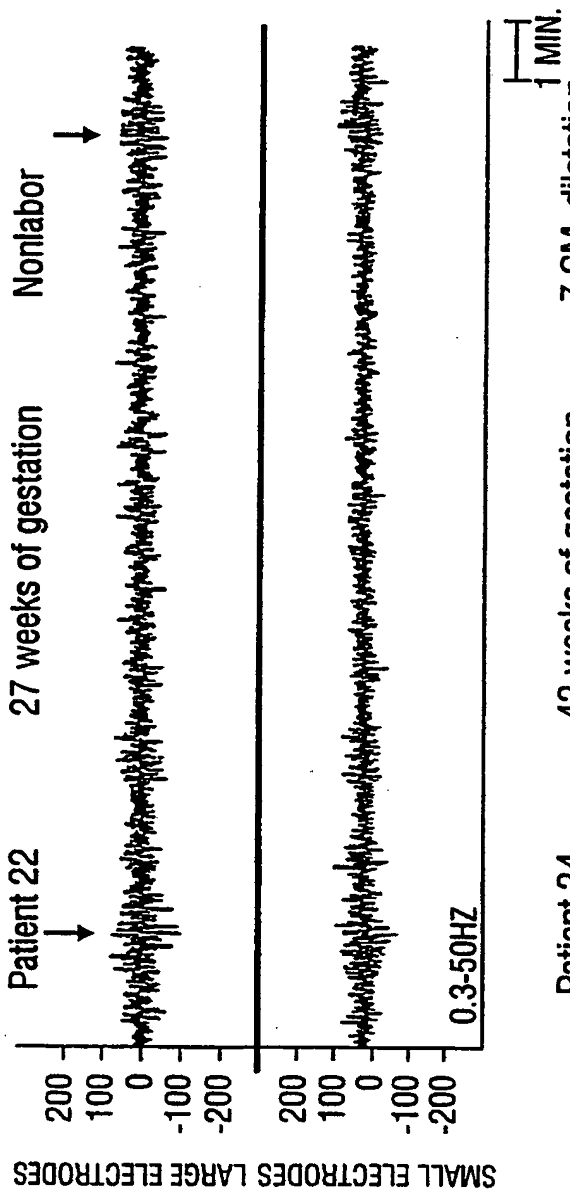


FIG. 23A

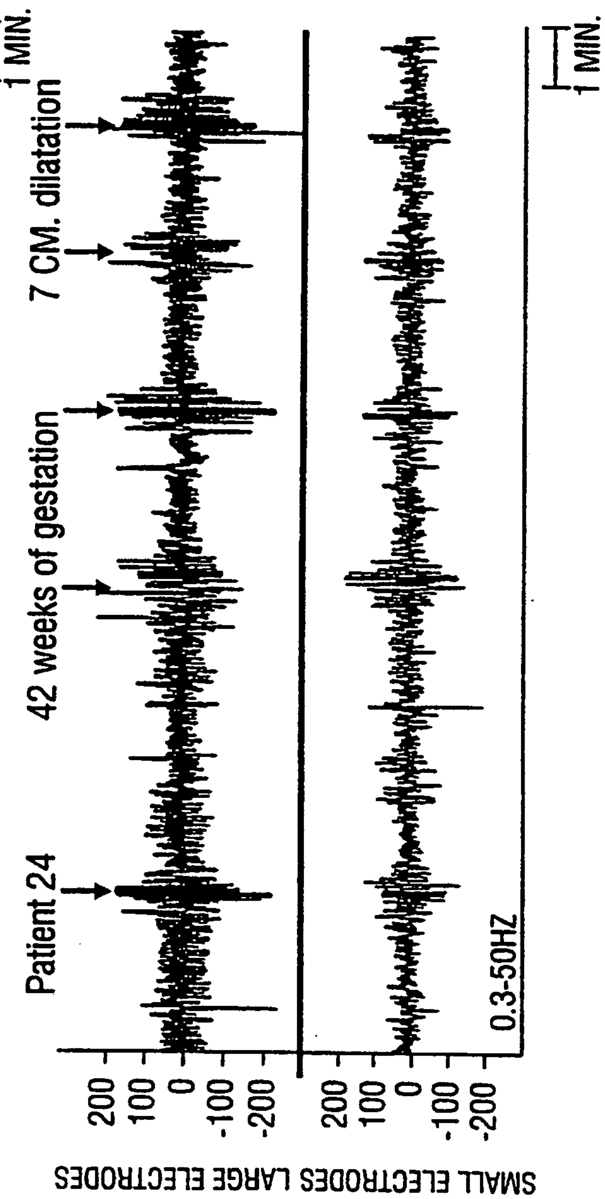


FIG. 23B

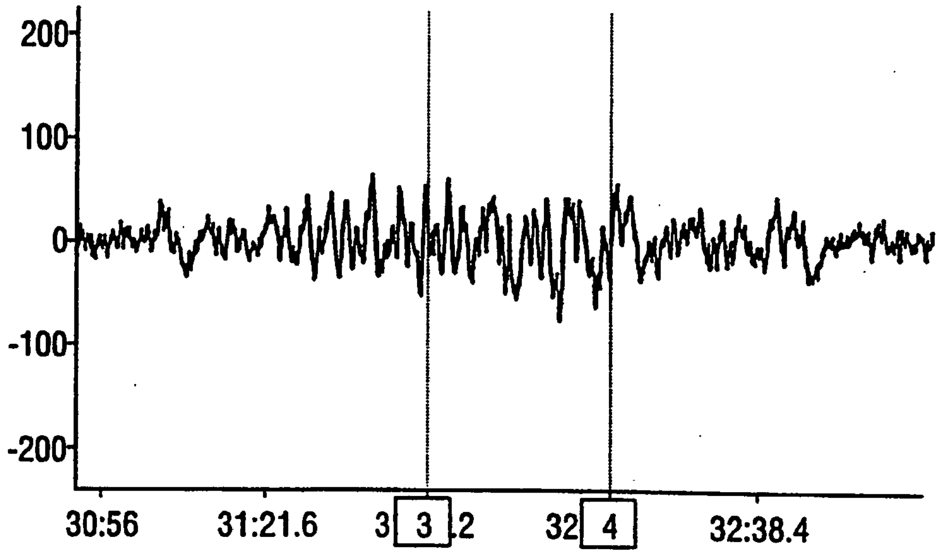


FIG. 23C

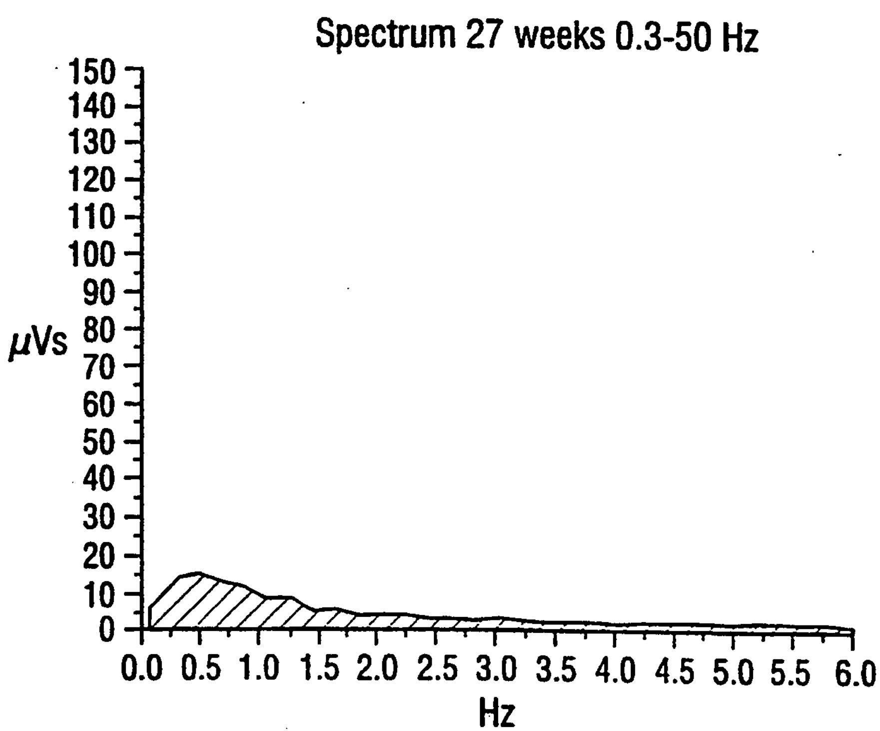


FIG. 23D

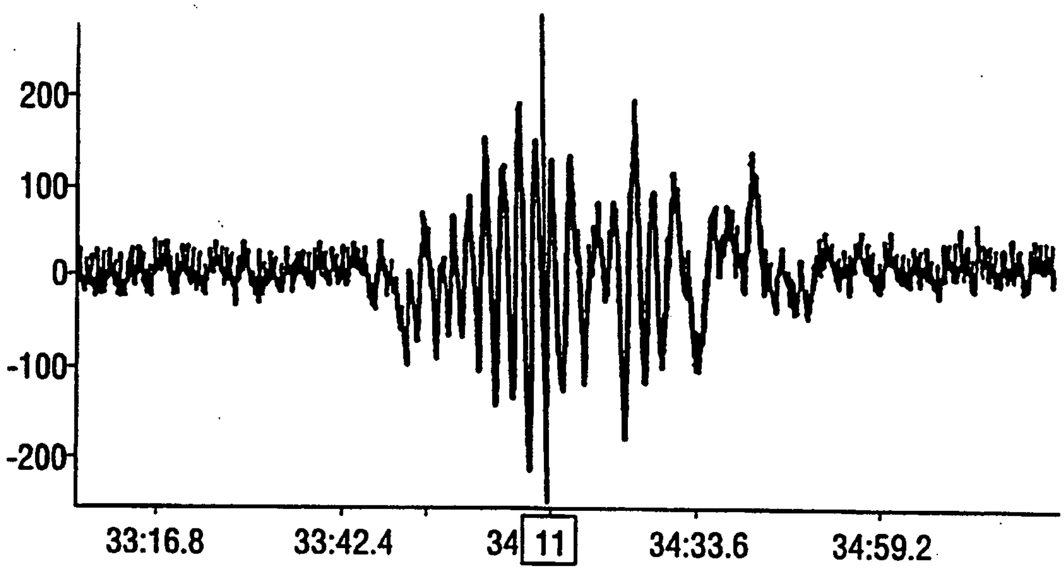


FIG. 23E

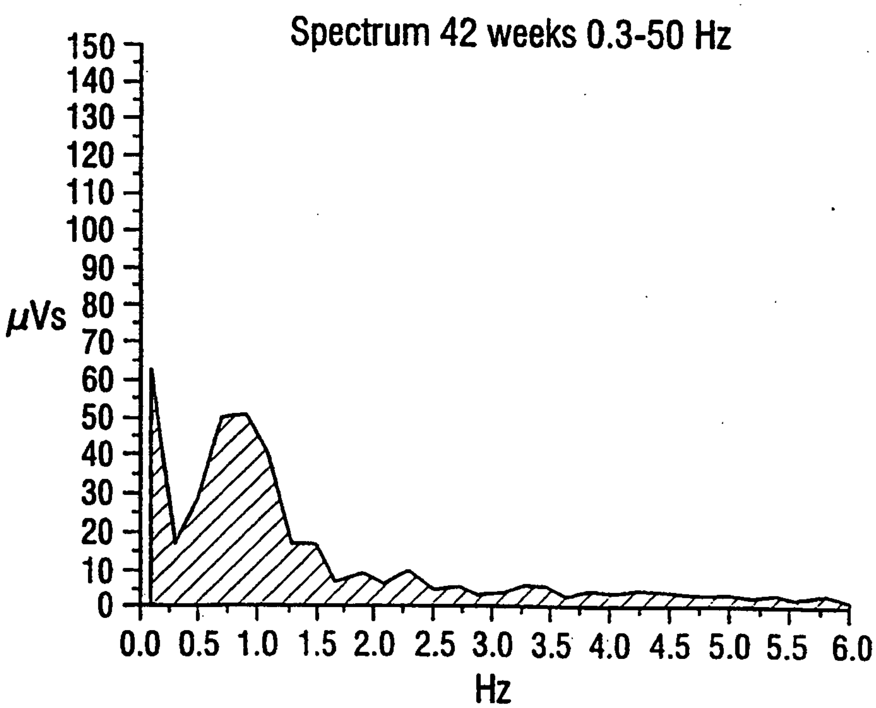


FIG. 23F

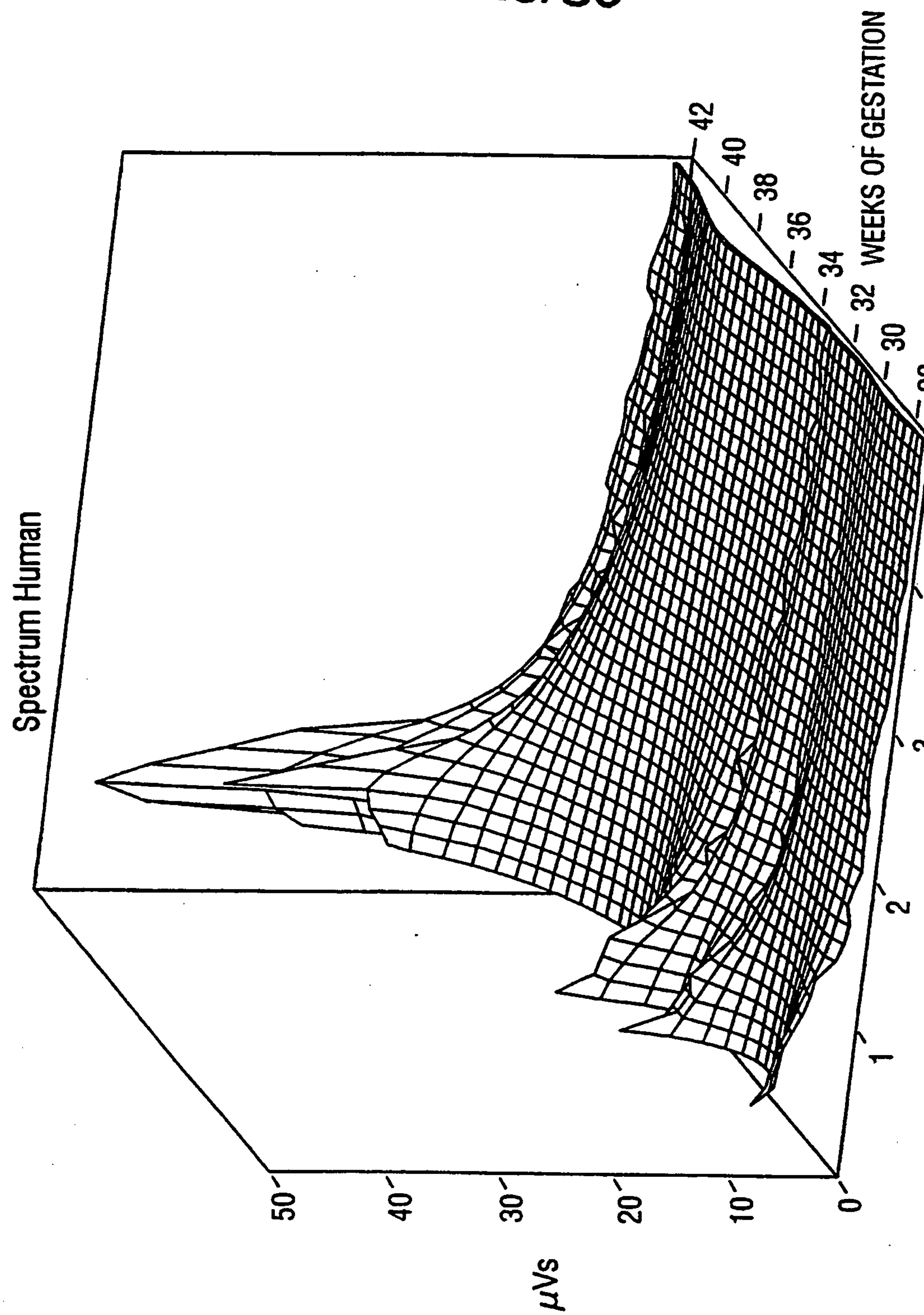

Spectrum Human
μVs
0
10
20
30
40
50
Hz
1
2
3
4
5
WEEKS OF GESTATION
28
30
32
34
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FIG. 23G

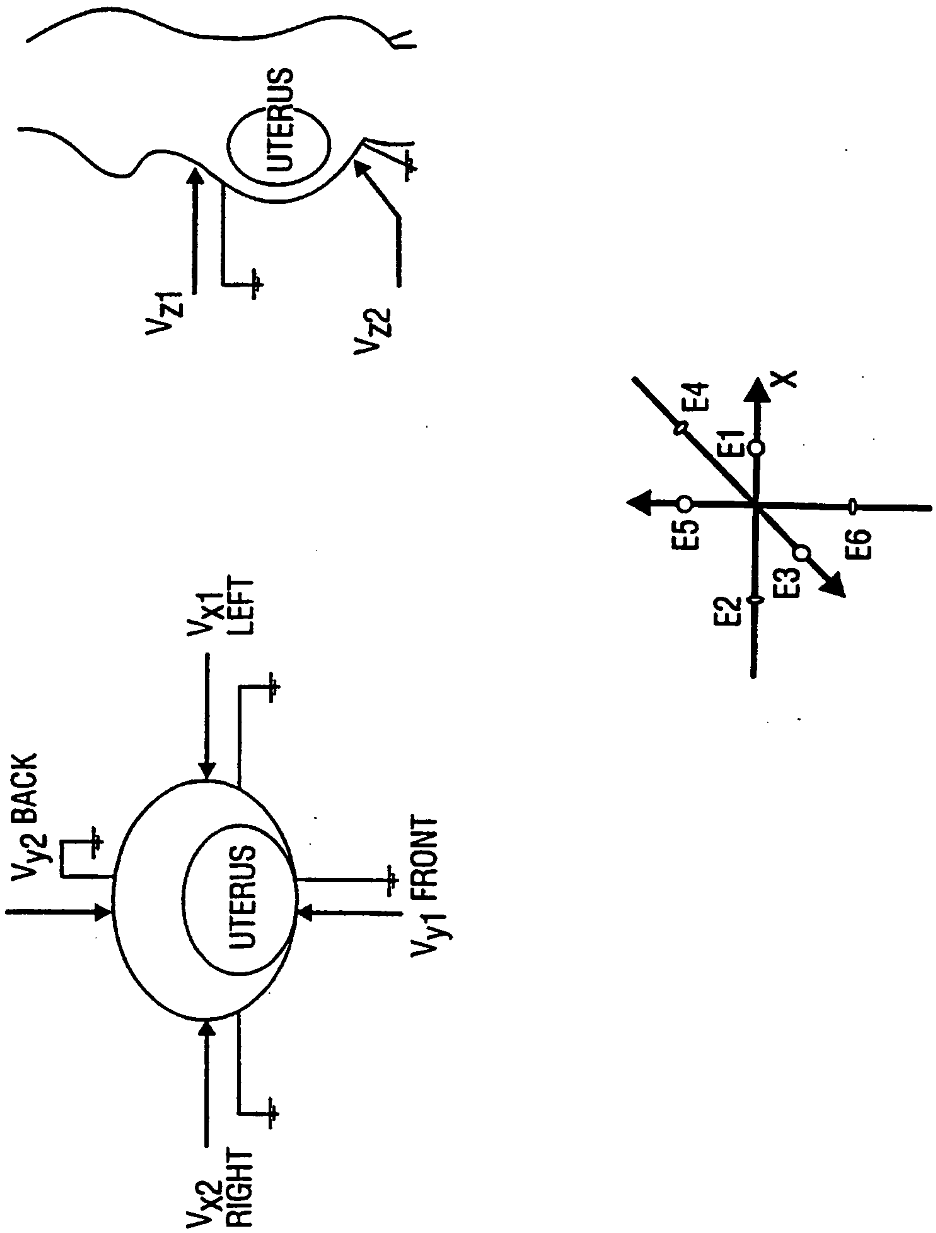
UTERUS
VZ1
VZ2
X
E4
E1
E5
E6
E3
E2
VX1 LEFT
Vy2 BACK
UTERUS
Vy1 FRONT
VX2 RIGHT

FIG. 24

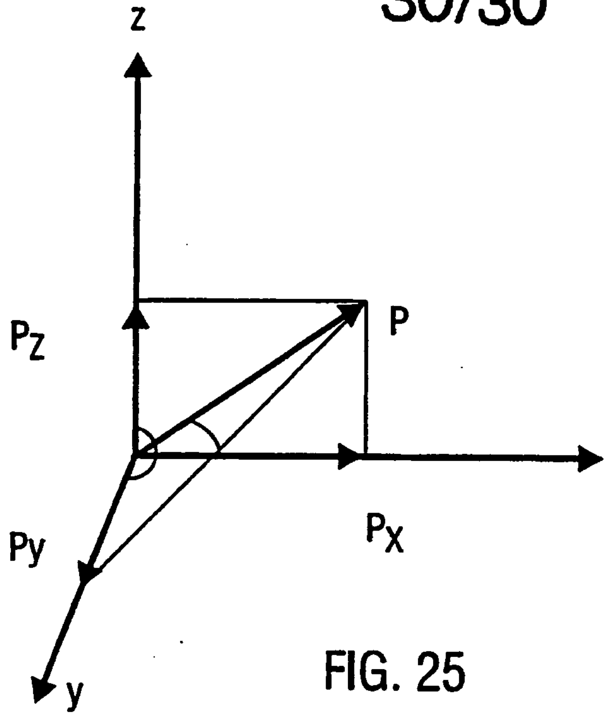

FIG. 25

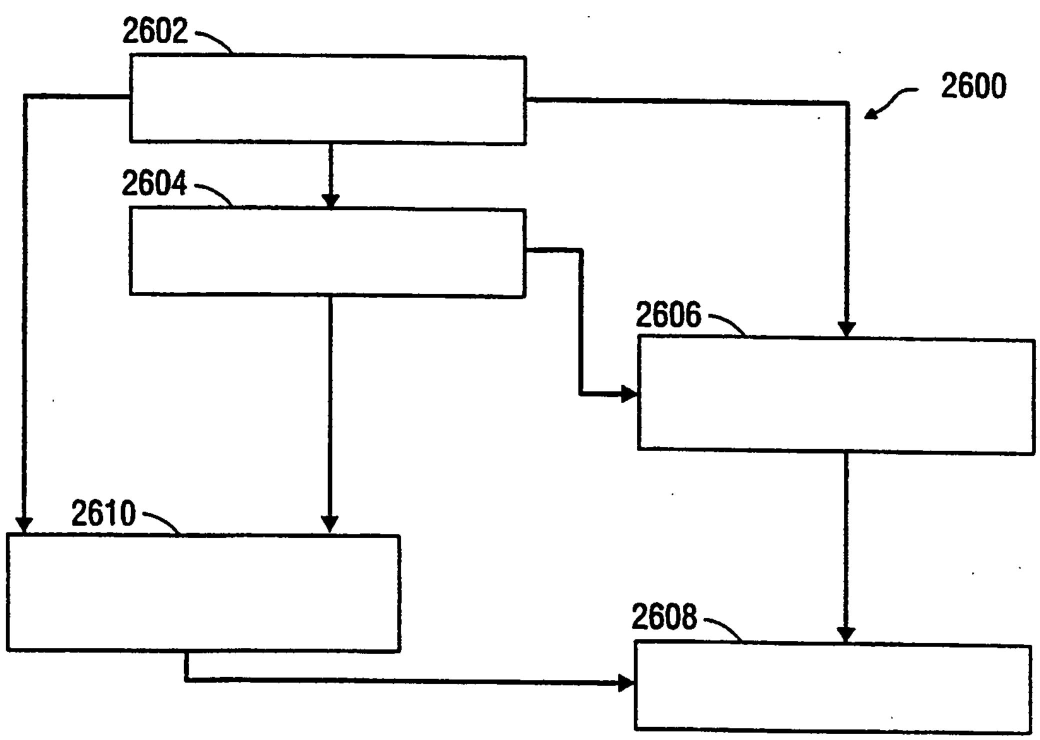

FIG. 26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/08777

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A61B 5/0488
US CL :128/733
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 28/733, 738, 774, 775, 778, 782

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A, 5,373,852 (HARRISON ET AL.) 20 December 1994.	1-31
A	US, A, 5,301,680 (ROSENBERG) 12 April 1994.	1-31
A	US, A, 4,967,761 (NATHANIELSZ) 06 November 1990.	1-31
A	US, A, 4,256,118 (NAGEL) 17 March 1981.	1-31

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be part of particular relevance

"E" earlier document published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
06 SEPTEMBER 1996	04 OCT 1996

Name and mailing address of the ISA/US	Authorized officer
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